VOLUME 35 NUMBER 3 MARCH, 1952

AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

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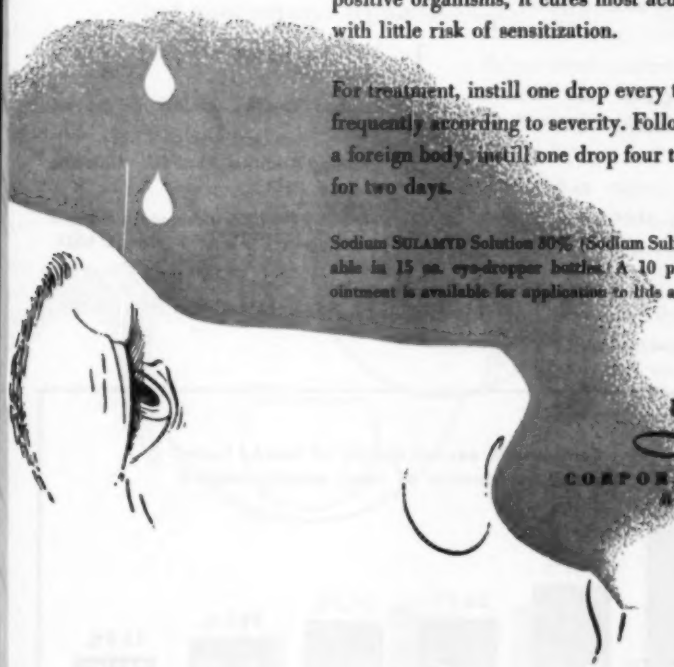

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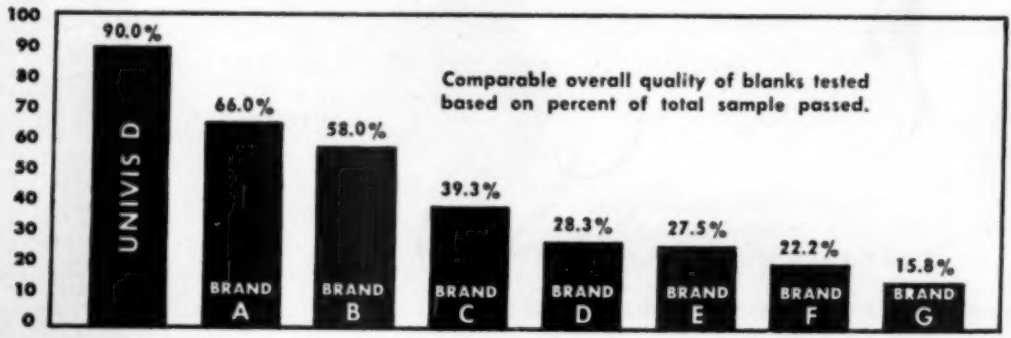

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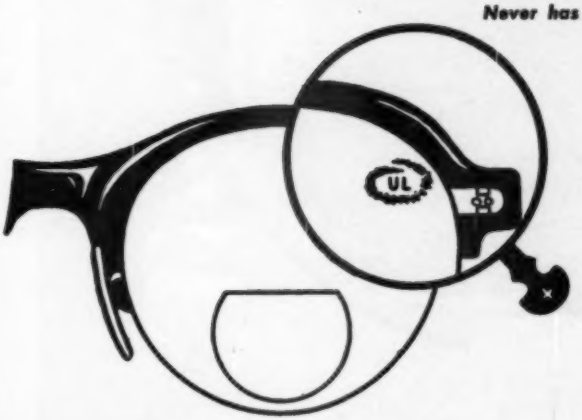

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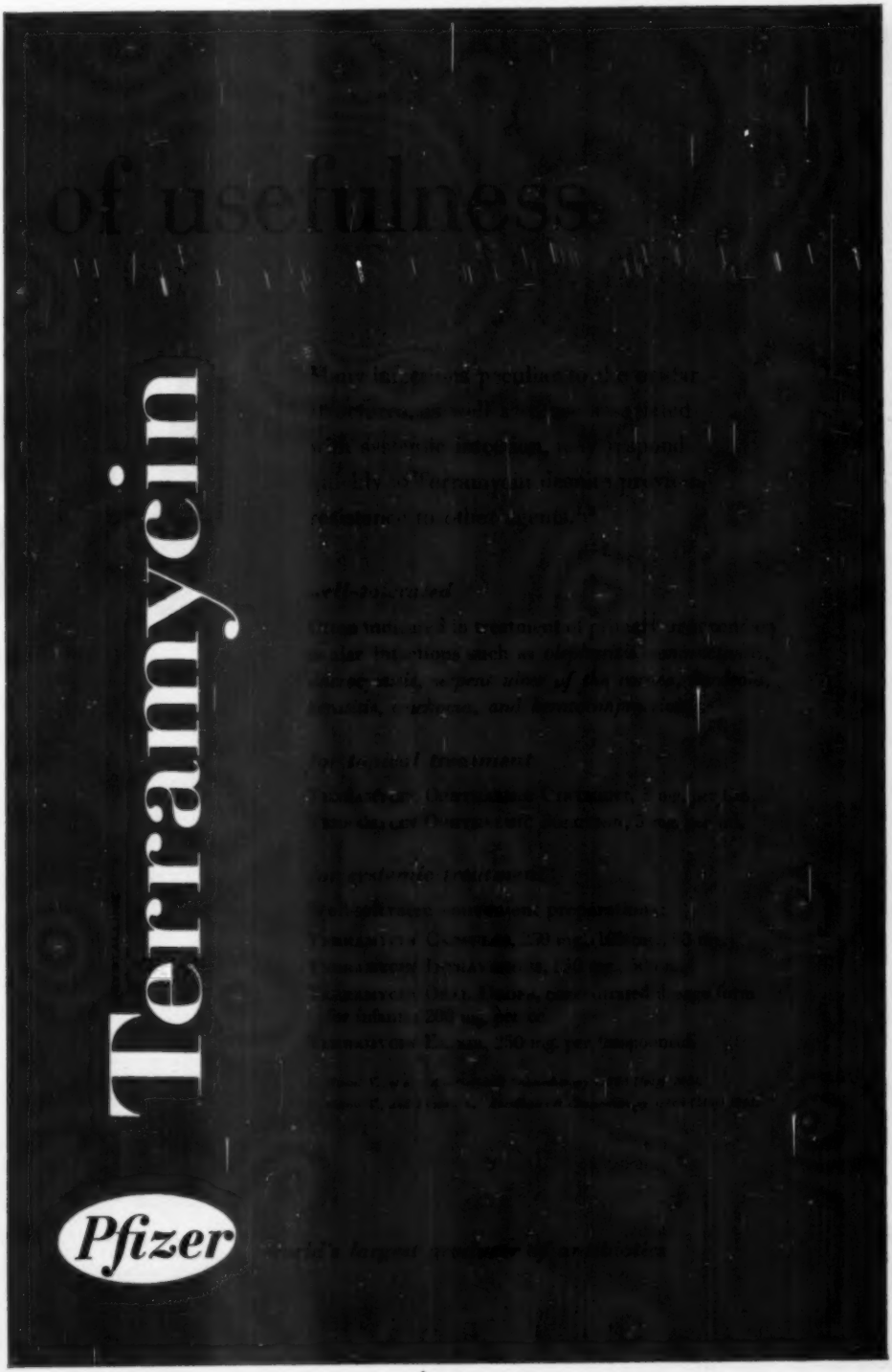
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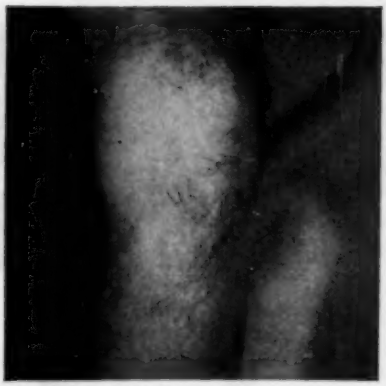

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Ward, L. E., Slocumb, C. H., Polley, H. F., Lowman, E. W., and Hench, P. S.: *Proc. Staff Mtgs., Mayo Clinic* 26: 361, September 26, 1951.

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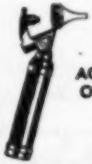

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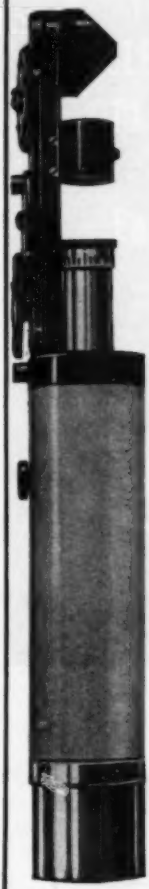

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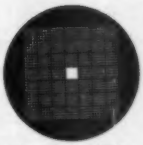

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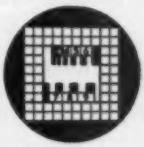

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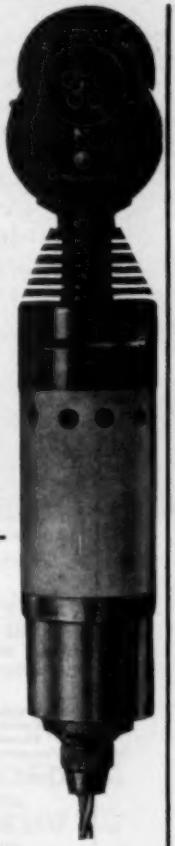

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[1] Crook, P., Carpenter, C. C., Klein, P. F. Science 112: 636 (12-1, 1950)
[2] Keeney & Broyles. Bull. J. Hopkins Hosp. 73: 329, 479 (1943)
[3] Theodore, F. H. Use of Propionates in Ophthalmology, Arch. Ophth. 41: 94 (Jan. 1949)

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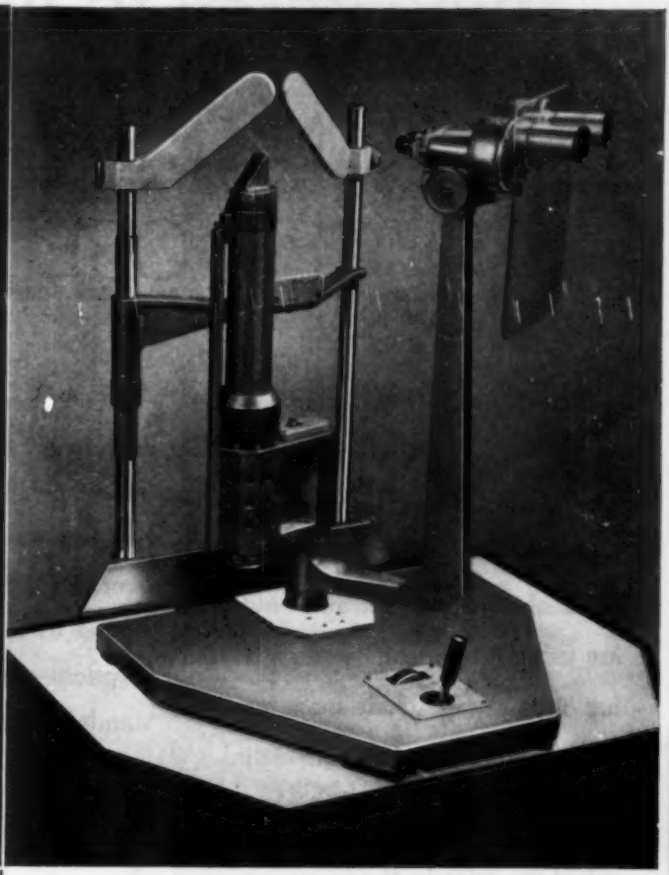

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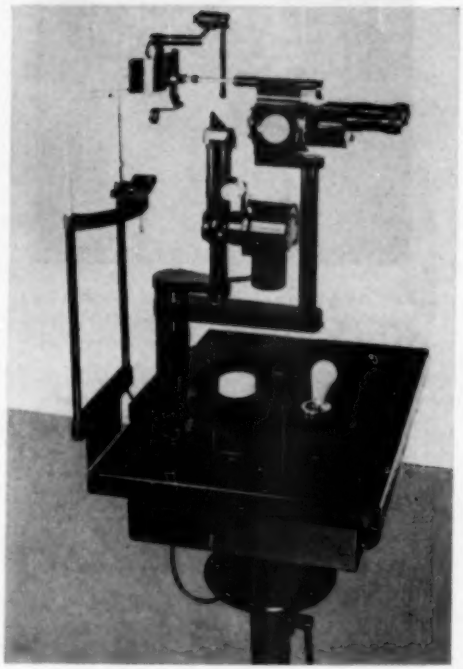

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RETROLENTAL FIBROPLASIA*

ETIOLOGY AND PROPHYLAXIS

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Retrolental fibroplasia is a disease of premature infants which usually becomes apparent during the first few days or weeks of life and often leads to partial or complete loss of vision. No attempt will be made in this paper to describe the clinical course or the pathology, as these have been well described by Terry, Owens and Owens, Reese, and others. I shall attempt, however, to show that retrolental fibroplasia is a terminal stage of uncompensated anoxic retinopathy in prematures, and that it is directly related to the oxygen environment of prematures.

The following research was done at the Christian Welfare Hospital of East Saint Louis, Illinois, with the kind and very able assistance of Miss Maybelle Parker and her staff of nurses. The premature center located here has an average daily census of 25 to 30 babies and admits well over 300 infants under five pounds of weight yearly.

During the year of 1950, 347 premature infants were admitted and treated. Of this number, eight† are known to have become blind presumably from retrolental fibroplasia.

In 1951, to October, 263 prematures were admitted. To date, we know of 20† who have developed this disease with partial or complete loss of vision. One significant difference in care of these premature infants during 1950 and those during 1951 suggests a relationship between the length of time a child spends in an incubator, the rapidity with which he is removed from an incubator, and retrolental fibroplasia. During 1951, the average stay of the prematures in incubators was shortened and the weaning off period reduced from seven to three days.

A study of all of the records of prematures admitted during 1951, however, revealed that those who did not develop retrolental fibroplasia were kept, on an average, 20 days in incubators; those who did develop the disease were kept for an average of 30 days. On casual study, this very contradictory finding might seem to indicate that retrolental fibroplasia is in no way related to the length of time a child is kept in an oxygen incubator. If we consider, however, the usual pediatric criteria which are used to determine when a child is to be placed in a normal atmosphere, it becomes immediately apparent that the group of children who developed retrolental fibroplasia were actually more oxygen deficient than the others.

During the past six months, two sets of twins and one set of triplets came under our observation. Of these, two of the triplets and one child from each of the twins developed the disease to the most severe extent. The amazing thing was that, of the twins and the triplets, the less likely to survive did not develop the disease, and the only difference in care was the administration of oxygen for a longer period of time to the weaker child.

* From the Department of Ophthalmology, St. Louis University. Presented before the St. Louis Ophthalmic Society, October, 1951. This paper is the elaboration of the preliminary report published in the JOURNAL, 34:1649-1650 (Dec.) 1951.

† Incomplete statistics.

TABLE 1

ANALYSIS OF CASES OF RETROLENTAL FIBROPLASIA

Birth Weight	Days on O_2 Since Birth	Time Changes Appeared After Oxygen Discontinued				Days off O_2	Add. Days O_2 Treat.	Results
		Vasodil.	Visible Neovasc.	Hemorrh.	Edema &/or Elevation			
2 lb. 10 oz.	19	1 day 2+	2 days	3 days	Peripheral edema, 3 days	3	25	Discharge; Subsequent exam. neg.
3 lb. 7 oz.	19	1 day 2+	3 days		Ex. periph. edema, 3 days	3	16	Discharge; Subsequent exam. neg.
4 lb. 10 oz.	7	1 day 2+	3 days		Periph. edema, 2 days; elevation in 3 days	3	27	Discharge; Subsequent exam. neg.
3 lb. 1 oz.	19	1 day Slight; 8 days-2+	2 days	1 day	8 days	10	50	Normal fundi
4 lb. 4 oz.	9	1 day Slight; 2 days-2+	3 days	3 days	2 days, edema & elevation	3	27	Discharge; Subsequent exam. neg.
4 lb. 13 oz.	11	1 day 2+		9 days	1 day, edema		None	Discharge; Subsequent exam. neg.
3 lb. 12 oz.	5	4 days 2+			3 days, edema		None	Discharge; Subsequent exam. neg.
4 lb. 4 oz.	10	1 day 2+	1 day	1 day	1 day, edema	8	19	Discharge; Subsequent exam. neg.
2 lb.	28	1 to 2 days-2+		1–2 days	2+ in 1–2 days		None	Discharge
3 lb. 15 oz.	30	1 day 2+	1 day	8 days	1 day, edema 8 days, elevation	8	22	Normal fundi
2 lb. 15 oz.	48	1 day Slight; 2 days-2+	2 days		1 day, edema		None	Normal fundi
4 lb. 4 oz.	32	1 day 2+					None	Normal fundi
3 lb. 5 oz.	29	1 day Slight					None	Normal fundi
3 lb. 11 oz.	30	1 day 2+	1 day	4 days	1 day	5	Now on O_2 at 45%	Much improved
3 lb. 4 oz.	13	1 day 2+	4 days		2 days		None	Discharge; Normal fundi
3 lb. 6 oz.	13	1 day 2+					None	Discharge; Normal fundi
4 lb. 12 oz.	4	1 day 2+			1 day		None	Discharge; Normal fundi
4 lb.	31	4 days 2+	2 days		2 days	10	On O_2	Much improved
3 lb. 10 oz.	24	2 day 2+	2 days		2 days, edema		None	Discharge; Normal fundi

In view of the above, the following was done:

PROCEDURE I

Fundi of premature infants were studied with particular attention to the size, tortuosity of retinal vessels, hemorrhages, new vessels, and the presence of grayish masses or areas. It was noted that, as a rule, the apparently normal premature infant, while in oxygen, had retinal vessels, either small or attenuated in caliber (frequently threadlike), which were not tortuous.

Grayish areas were often noted in the extreme periphery. These areas were not grayish white and did not appear edematous. Not a single case was seen at this hospital which could be called early retrolental fibroplasia in any prematures while they were in an incubator with an *adequate* oxygen supply.

Since reporting my preliminary findings, I have seen infants in incubators suddenly develop engorged retinal vessels and peripheral edema with early neovascularization when they were apparently being supplied with a proper amount of oxygen. Two of these babies even progressed to the point of developing retinal hemorrhages. Investigation, however, revealed in every case a human or mechanical failure which grossly affected the oxygen supply to these children. When the deficiencies were corrected, all of the changes regressed. I shall discuss these factors later.

The prematures who were no longer in oxygen (excluding those diagnosed as having retrolental fibroplasia or early retrolental fibroplasia), as a rule, were noted to have vessels which could be called full or engorged.

On reviewing my notes on those prematures who developed retrolental fibroplasia, I was amazed to find that, in all, the earliest signs of the disease were noted shortly after the child was removed from an incubator.

PROCEDURE II

Nine cases of early retrolental fibroplasia were treated by placing the infants in oxygen incubators. All had marked vascular tortuosity and neovascularization; eight had marked vascular engorgement; five had retinal hemorrhages; and four had definite retinal elevation. In all cases the disease was immediately arrested.

Of these infants, five have already been discharged—three have fundi with no evidence of any damage; one has only tortuous and numerous vessels as an aftermath; the third shows some white peripheral patches and otherwise normal fundi. The four remaining cases are still under observation and treatment only because a sudden change in temperature in this area affected our oxygen source in an unforeseen way.

When the cases of retrolental fibroplasia were first treated, we depended entirely on gauges which measured the oxygen flow in liters. All of the nine cases were supplied oxygen at the rate of four to six liters per minute. When, however, we found one case which though arrested did not seem to improve, we began measuring the actual oxygen concentration. To our surprise we found that some of our old incubators with oxygen flowing at eight liters per minute had actually a concentration lower than new incubators receiving one or less liters per minute. We also found that the position of the incubator in the nursery greatly affected its oxygen concentration—those exposed to drafts or air currents tended to have a lesser concentration than the others.

Then we began to measure oxygen concentrations in all incubators routinely and tried to adjust the concentration at about 60 percent. When we thought that this problem was solved, unaccountable regressions and then improvements began to be noticed in several of our cases. After investigation, we found that the problem of keeping an infant properly supplied with oxygen is quite complex. Following are some of the factors which enter into it:

1. *Opening the lids* of our incubators to feed or change the child caused an almost immediate drop of oxygen concentration to

slightly above room level. This may be an important factor, especially if the child is a slow feeder, as it means that for 20 or more minutes he is in an environment to which he is not accustomed.

In five to 10 minutes after the lid is closed, the oxygen concentration rises almost to its previous level. This means that an incubator can be entirely without any oxygen supply for any period of time and yet show a proper oxygen concentration if the supply is restored 10 minutes prior to measurement.

2. *Faulty valves.* On at least two of our outlets the valves were so defective that slight accidental pressure of the incubator against them caused them to close and remain closed till opened manually.

3. *Vents.* Accidentally opened vents caused a marked drop in oxygen concentration.

4. *Tubing.* Accidentally pinched off or entirely disconnected tubing is not at all an unusual accident in a busy nursery.

5. *Tanks allowed to empty* are sometimes not changed immediately because of other pressing duties.

6. *Sudden change of temperature* if the oxygen supply tanks are kept outdoors. Some of our incubators are supplied with oxygen directly from tanks kept in the nursery. Many, however, are fed from a pipe which is connected to a series of oxygen tanks stored outdoors. Almost every time the weather turned cold there was a noticeable fall in the amount supplied to our nursery. Unfortunately, this usually happened at night when we had insufficient help to keep careful check and we were unaware of this for some time. What actually happens when the temperature drops has still not been discovered. It has been suggested that contraction of the metal pipe and joints might cause a leakage which is not apparent at other times.

We were made keenly aware of the effect of temperature on our oxygen source by the following events:

I was called early one cold morning following a severe snow storm and informed that the oxygen concentration in many of the incubators had fallen precipitously and that probably some of the incubators had not received any oxygen at all for some time. On examining the children that noon, I found that the four under treatment for retrolental fibroplasia showed severe hemorrhages and moderate to marked retinal detachments. (Several others not under treatment showed less severe changes.) Forty-eight hours previous to this, I had examined these same children and was well pleased with their progress.

Since, at the time of my examination the oxygen from our outside source was again flowing properly, I was under the impression that it was the snowfall which had interrupted our supply in some unknown way. For the next several days, however, we noted at times improvement and then regression in our cases, especially in the four under treatment.

Investigation then revealed that, during the day when the temperature was not too low, there was no difficulty in keeping a proper concentration of oxygen in our incubators. At night when often the temperature would drop quite low, it became very difficult to keep up a proper flow of oxygen. By the time we became aware of this, the four infants with retrolental fibroplasia had progressed to the point that all had marked detachments and two such severe detachments and hemorrhages that I almost gave up hope that anything could be done for them. Yet, when the nurses were instructed to open routinely the oxygen valves more during the night, three of the four cases showed remarkable improvement, and of the two with marked detachments one showed marked regression while the other, because of organizing vitreous bands developed marked bilateral but not total detachments.

Of the five infants discharged, one developed an upper respiratory infection two and one-half weeks after discharge, and the other a bronchopneumonia at an unknown time after release from the hospital. In both, there was a reappearance of vascular engorgement and peripheral edema. One even developed fresh retinal hemorrhages. In both,

however, the changes regressed as the child recovered from his illness.

One of the first changes noted when a child was placed on oxygen therapy was attenuation of the caliber of the vessels. In some cases, within 24 hours, a dramatic constriction took place. Then the grayish white areas and elevations began to regress and the hemorrhages slowly became absorbed. Gross hemorrhages absorbed very slowly, and the areas anterior to them persisted to appear edematous for a long period of time.

Those cases which were not treated until there was very marked vascular engorgement and tortuosity showed the greatest immediate vascular response but later, after several days of treatment, the vessels again became moderately dilated and the tortuosity became more evident (in retrospect, this subsequent dilatation may have been due to our inability to keep a constant oxygen level in the incubators).

In no case did new hemorrhages, gray-white patches, or retinal separation develop while the oxygen supply was adequate.

During the period of time when several of the infants were subjected to marked lowering of their oxygen environment, I was impressed by the tremendous dilatation of the retinal vessels, exudation into the vitreous, the patchy edema along many veins, and the number of hemorrhages some of which were so distributed along each side of a vein as to suggest generalized leakage.

I was also impressed by the fact that those prematures who were placed on oxygen after being allowed to develop only the early signs of retrolental fibroplasia showed much less severe changes. This suggests that, once a child has developed the retinopathy of anoxia, he becomes much more sensitive to sudden changes in his environment.

Procedure III

After I was convinced that the changes in early retrolental fibroplasia were reversible, 19 prematures, whose general condition made it safe to take them out of incubators, were suddenly removed from oxygen.

The first eight were removed from incubators receiving oxygen at four or more liters per minute (concentration unknown but probably high) and placed in a nursery where the oxygen concentration at the time was between 22 and 25 percent. (The weather was warm and windows more frequently open.) The others had their oxygen concentration while in incubators gradually reduced until the concentration was about 40 percent; then they were placed in a nursery where the concentration varied, at the time, from 25 to 29 percent.

None of these children showed difficulty in breathing, change in color, or disposition. Clinically, they appeared to meet their requirements for oxygen from the usual concentration found in the nursery.

The fundi of all were examined on the day oxygen was to be discontinued and almost daily afterward. Within 24 to 48 hours, all cases showed dilatation of the retinal vessels. In 15 cases this dilatation was marked —at least two to three times average size.

Of the four cases which initially showed only slight dilatation, one developed engorged vessels within four days and another in eight days. Of the two infants who failed to show a marked vascular response, one developed peripheral neovascularization in two days. In 12 cases visible peripheral neovascularization developed within one to four days. Eight infants developed retinal hemorrhages in one to 10 days, while in 16 cases peripheral retinal edema developed—some with definite elevation—in one to eight days.

Of this number, nine babies had to be placed back into incubators with oxygen within three to 10 days because of the alarming progression of the retinal changes (progressive vasodilatation, tortuosity, neovascularization, and peripheral edema).

Without exception, all cases showed marked improvement within 24 hours and in three to four days the fundi were almost normal in appearance. Hemorrhages were rapidly absorbed and the peripheral edema and elevation disappeared, sometimes in 24 hours. Some of these children showed re-

gression during the period that control of the oxygen concentration became difficult but in only one case was regression very marked. Seven babies have been discharged with normal appearing fundi after spending 19 to 50 additional days in an incubator. The two still in incubators are recent cases.

All of the remaining infants recovered spontaneously and were discharged. (They were, however, in the nursery where the oxygen concentration was consistently above 25 percent and sometimes as high as 29 percent.) Two of this latter group subsequently developed mild anoxic retinopathy under the following circumstances:

The first child was discharged with entirely normal fundi. Five days later, on examination in the office, it was found that the retinal veins were engorged and there was a fresh blotchy hemorrhage in the left temporal midperiphery. On questioning, it was found that the home was warmed by a fuel oil stove and that all windows were kept closed. I advised that a window be kept open in the baby's room. Three days later the fundi were much improved and the hemorrhage partially absorbed. Subsequent examination revealed normal fundi.

The other child was also discharged with essentially normal eyes. About two weeks later, the baby developed an upper respiratory infection with respiratory difficulty. I noted fresh, small, blotchy hemorrhages in the superior temporal midperiphery of the left eye, with retinal edema anterior to them, and prominent vessels in the periphery. These changes regressed as the child's illness improved.

Clinically, the disease appears to develop in the following way:

First the retinal vessels dilate; then tortuosity in the vessels begins to develop, starting in the periphery and midperiphery (occasionally, the formation of many fine new vessels in the periphery and rarely even in the posterior pole is the most prominent initial change).

At about the same time, grayish-white areas become evident peripherally. These areas may occupy the entire periphery or localize in one or more sectors. I have often noted that, if localized in one segment, the vessels leading to it are particularly dilated and become very tortuous as they approach it. As the disease progresses, the vessels become more dilated and more tortuous. Many new and very tortuous vessels become visible, the grayish-white areas progress toward the posterior pole and become elevated. Hemorrhages may or may not develop.

Procedure IV

Four babies with far-advanced retrolental fibroplasia and with total or severe detachments were readmitted to the hospital and placed in incubators with oxygen. Their ages ranged from two months 28 days to five months. Oxygen was administered for periods varying from nine to 18 days. No definite improvement was noted in any case.

Prevention

When we first began to investigate retrolental fibroplasia, all of the prematures admitted to our center were administered oxygen at the rate of four or more liters per minute. This rate of administration caused a concentration of oxygen in the incubators ranging from 54 to 84 percent.

It soon became evident to us that those children who had become accustomed to breathing in high concentrations of oxygen had to be weaned off oxygen at a slow and gradual rate. Any significant drop in their oxygen supply caused an appearance of vasodilatation and peripheral edema.

It was also observed that several prematures weighing over four pounds,* who were not given oxygen while developing the usual vasodilatation and peripheral retinal edema, showed less severe reactions than other prematures weighing over four pounds, who had become acclimated to a high oxygen concentration and then were removed from it.

We came to the conclusion that a child who has been subjected to high concentra-

* Most prematures over four pounds in weight show little or no fundus changes when *not* placed in an oxygen-enriched atmosphere.

tions of oxygen for any prolonged period of time must undergo a period of acclimatization similar in some respects to that an adult experiences when he is placed from a low to a high altitude. I believe that any significant lowering of the oxygen concentration to which the infant is exposed causes a similar drop in O_2 blood tension until certain compensatory physiologic changes take place.

At the present time we are approaching the problem of prevention thus:

Prematures weighing over four pounds who show no signs of anoxia are not placed in oxygen. Their fundi, however, are watched carefully and, if signs of progressive anoxic retinopathy develop, they are placed in incubators with oxygen at a relatively low concentration (40 to 45 percent).

Prematures under four pounds are placed in an oxygen atmosphere of about 45 percent, or lower if possible, unless for some reason or other a higher concentration is indicated. They are weaned off slowly. (We still do not know the optimum concentration or time that a child should be in an incubator.) When removed from the incubators they are placed in the nursery where, at this time, the oxygen concentration varies from 25 to 29 percent.

On making this change, the majority of the children respond by showing some vascular engorgement and some peripheral retinal edema. When the changes regress, they are either discharged or placed in a nursery where the oxygen concentration is about 21 percent (depending on how fast the changes regress).

Those cases which show progression of retinal changes are placed in incubators and the oxygen concentration adjusted to about 45 percent (occasionally a higher concentration is required). When the fundi appear normal, the weaning off process is begun.

Anoxia

There is sufficient evidence to indicate that prematures do have a relative oxygen deficiency and that they do benefit from oxygen administration. This oxygen deficiency may be caused by: (1) Subnormal pulmonary ventilation, (2) thickened alveolar walls (interference with gaseous diffusion), (3) presence of a fetal hemoglobin which takes up oxygen more readily than adult hemoglobin but releases it less readily to the tissues, (4) anemia of prematurity.

There is also sufficient evidence to show that anoxia of itself can cause vascular damage and hemorrhages. Post-mortem studies of infants dying of severe oxygen deficiency, as in asphyxia, show generalized petechial hemorrhages. According to Cruickshank, oozing from the meninges was found to be almost universal in infants that died from the effects of asphyxia.

Potter and Adair have stated that the characteristic post-mortem finding in infants who have died of primary anoxia are discrete petechial hemorrhages in the lungs or thymus and/or petechial hemorrhages in the brain substance.

They also state that "asphyxial hemorrhage is always smaller in amount than that produced by trauma. It is probable that severe cerebral congestion and extravasation of erythrocytes into the subarachnoid space are due to capillary injury produced by anoxemia rather than to local trauma. This is also true of hemorrhage into the lateral ventricles. Microscopic hemorrhages in the brain substance are found most frequently in the pons, in the medulla, and in the region of the lateral ventricles, and are similar in origin to petechiae produced by anoxemia in other parts of the body."

Munro and Eustis state, "Asphyxia should be given at least a temporary recognition as an etiologic factor in the production of intracranial hemorrhage in the newborn," and they add that the number of cases of intracranial hemorrhage which might properly be classed as traumatic in origin is relatively quite small.

There is also evidence that anoxia may cause serious damage to fetal tissues. Ingalls has proven that anoxia is a teratogenic agent. He has placed pregnant mice in a high altitude chamber at 25,000 and 27,000 feet.

Each mouse was placed in the chamber on one occasion only for a period of five hours. As a result of this kind of insult, a high percentage of the litter born showed a wide spectrum of defects in a wide variety of organs—depending upon the stage of gestation at which mother and litter were insulted. If, for example, pregnant mice were subjected to a lowered atmospheric pressure four to five days before delivery, a significant number of the litters showed the so called "open eye." (The mouse fetus normally has the eyes closed at birth.)

Physiologically, it is known that a normal adult cannot withstand a sudden transfer to an environment of lowered oxygen concentration without showing signs of disturbance of the central nervous system, and that the severity of these disturbances is proportional to the drop in oxygen tension.

It is also known that it takes several days for a normal adult to acclimate to an atmosphere of decreased oxygen pressure. It is unreasonable to assume that an infant can tolerate without harm a sudden change in oxygen environment from a concentration which may be as high as 80 to 90 percent to one of 21 to 22 percent, especially since we know that prematures react in an abnormal way to slight variations of temperature, humidity, diet, and infections. It is also unreasonable to assume that prematures can be safely acclimated to a normal oxygen environment simply by removing them from their incubators a gradually increasing period each day or by rapidly cutting down their oxygen concentration.

Conclusions

1. Retrolental fibroplasia is a terminal stage of a disease induced by:

a. Failure to keep an oxygen-deficient child for a sufficient length of time in an oxygen-enriched environment after birth, or

b. Failure to acclimate a child slowly to a normal oxygen environment. This is especially true if a child is kept in an oxygen incubator for long periods of time and even more so if the oxygen concentration in the incubator has been kept at a high level. We have found that children subjected to periods of high and then low oxygen concentrations so that early changes of anoxic retinopathy develop and regress become hyper-reactors to any sudden, even slight, lowering of their oxygen environment and have to be acclimated at an extremely slow rate.*

2. Retrolental fibroplasia is a terminal stage of anoxic retinopathy. This retinopathy is produced by retinal oxygen deficiency during a period of life when vascularization of the retina is still taking place and the retinal elements are not fully developed. It is known that the retina utilizes oxygen at a rate probably higher than any other tissue in the body. The premature retina may have an even higher requirement.

What happens is this: As long as enough oxygen is circulating in the blood stream, the retina develops normally, and the retinal blood vessels remain normal in size. As soon as oxygen deficiency in the retina develops, there is a compensatory dilatation of the retinal vessels and stimulation of formation of new vessels (vascularization of deeper layers of retina is known to take place at about the seventh month of the fetus). If enough oxygen is delivered by the dilated vascular channels to the growing retina to meet its demands partially or completely, the disease either does not develop or develops only in its attenuated form.

If enough oxygen is drained off from the circulating blood by the oxygen-hungry retina, perhaps the vascular walls begin to suffer, weaken, and allow transudation of serum and eventually of blood. The retina also, not being able to carry on normal metabolism, begins to become edematous. This edema would logically take place first in the periphery where it is known that full development takes place last.

The exudation from the blood vessels

* Even prematures, subjected to varying oxygen concentrations in incubators, who initially show no fundus changes, appear to respond in an abnormal way during the weaning-off period and have to be acclimated carefully.

would account for the vitreous opacities. The retinal edema and exudation of fluids may be responsible for the gradual detachment.

Similar changes probably take place in the ciliary body and iris, but because of the lesser requirements of oxygen, are not so marked. This would account for the color of the iris, the synechia which develop, and the eventual shallow chamber. Later atrophy with fibrosis sets in, and the fully developed picture is complete.

3. Let us not fail to grasp the full meaning of the pathologic process which takes place in retrolental fibroplasia. What we are actually witnessing with our ophthalmoscopes in the study of this disease is the response of immature neural tissue to slight anoxia.

It is illogical to assume that these changes of subclinical anoxia are limited entirely to the eye. We know that the brain and other nervous tissues also have a high oxygen requirement. We know that prematures often are slower in development, often are irritable, and often are mentally retarded. We also know that some areas in the brain (and endocrines) apparently lie dormant until a certain period and then undergo rapid development. Also the degree and stage of development of various centers at a given time vary in different infants.

Observation of the retina in retrolental fibroplasia shows that retinal edema most often appears first in the periphery and often is localized to one or more sectors strongly suggesting that these sectors are in a more fetal stage of development and require more oxygen. In fully developed cases of retrolental fibroplasia, often only one sector of the retina is destroyed.

It is my belief that the changes which take place in retrolental fibroplasia—this vasodilatation, edema, neovascularization, transudation from the blood vessels, hemorrhages, and then atrophy followed by fibrosis—may take place in all anoxic fetal tissues which utilize oxygen at a rapid rate not only in oxygen-deficient prematures but also in oxygen-deficient full-term babies.

We know that, at birth, the child gives evidence that certain nervous centers are well developed, some poorly developed, and others not functioning. He can, for example, move his arms and legs, cry, feed, and so forth, but he lacks coördination, is unable to sit, lacks balance, and so forth.

It is quite possible, and likely, that oxygen deficiency (even subclinical during a period of time when certain centers are actually undergoing rapid development affects these centers in the same way that the eye is affected in retrolental fibroplasia, and that oxygen deficiency is responsible for many intracranial hemorrhages, diseases such as cerebral palsy, certain cases of epilepsy, mental retardation, and certain metabolic and endocrine disorders.

It is quite possible, and likely, that many metabolic or nervous disturbances, which make their appearance several weeks or months after birth in a child apparently normal at birth, may be entirely due to arrested growth or pathologic alteration because of anoxia.

If this be true, anoxia in a fetus produced either by some disease interfering with oxygenation in the mother or child (uterine bleeding, placental anomalies, and so forth) would produce not only a clinical picture of retrolental fibroplasia but also anomalies involving other systems, the extent depending on the stage of development at the time of the anoxia.

Retinal dysplasia differs from retrolental fibroplasia only in that the eyes are affected when in a more fetal stage of development and that other organs, therefore, also show damage.

Congenital encephalo-ophthalmic dysplasia differs from the usual retrolental fibroplasia only in that the anoxia becomes manifest during a time when only the central nervous system and eyes are undergoing rapid development.

4. If, in some cases, such severe changes as hemorrhages and edema can be produced in an actively growing fetal tissue by subclinical anoxia of only 24 hours' duration, the

conclusion seems justified that any evident anoxia must be much more damaging. Even if the changes induced by anoxia do not progress to their full completion, a single hemorrhage in a vital center may so damage that center that irreparable harm is done.

Inevitable are the conclusions that:

1. Any condition or disease during pregnancy or early infancy which interferes with the proper oxygenation of the blood is extremely serious to the future welfare of the child.

2. Drugs, narcotics, and anesthetics, used before or during delivery, which will depress respiration or interfere with oxygenation in the mother or child must be reconsidered and reëvaluated at once.

3. A baby blue at birth is potentially a seriously injured child.

Summary

1. Retrolental fibroplasia is an example of a response of immature neural tissue to anoxia. This anoxia may exist primarily because of inadequate oxygenation of the blood or be induced by exposing a premature to an environment of higher oxygen concentration and withdrawing him so rapidly that the physiologic changes of acclimatization cannot take place before irreparable harm is done to rapidly developing areas—such as the retina of the eye.

2. Retrolental fibroplasia is preventable by the proper administration of oxygen. Prematures should be given minimal amounts of oxygen—just sufficient to meet their needs—and weaned off slowly. Excessive oxygen concentrations should be avoided.

3. Anoxia can cause serious pathologic alteration in rapidly growing fetal tissues. The type of damage produced depends on the stage of development during which the anoxia becomes manifest.

4. Nontraumatic intracranial hemorrhages in the newborn, cerebral palsy, certain cases of epilepsy, mental retardation, certain endocrine disturbances may be entirely due to anoxia during a period of time when certain centers are undergoing rapid development.

5. Any condition interfering with oxygenation during pregnancy or infancy must be considered extremely serious.

6. Any method of delivery which produces anoxia in a baby should be scrupulously avoided.

Addendum

All of the four original cases of retrolental fibroplasia treated with oxygen, who had suffered during the time oxygen control became difficult, have been discharged. The marked retinal detachments in the most seriously damaged baby persisted.

About two days after the other three were removed from an oxygen-enriched atmosphere of 25 to 28 percent, one developed a peripheral retinal detachment in one eye (the other eye remained ophthalmoscopically normal except for pronounced granular pigmentation); one baby developed a large blotchy hemorrhage in the posterior pole of one eye and subsequently a flat detachment of the temporal midperiphery and periphery (the other eye remained ophthalmoscopically negative); the third child showed no reaction except moderate vascular dilatation and, at the time of discharge, had a small peripheral retinal fold in one eye and a white, atrophic-appearing patch in the extreme temporal periphery of the other eye.

Since starting this work, I have not seen a single case of early retrolental fibroplasia develop which was not due to oxygen lack and none which did not improve when oxygen was administered. Nor have I seen a single case of blindness or partial blindness in any prematures in the last 100 consecutive premature babies attended.

215 Metropolitan Building.

Acknowledgement

My sincere thanks are expressed to Dr. B. B. Berman, Dr. William E. Knause, Dr. U. S. Thimsen, Dr. G. Van Dusen, and Dr. D. Rawling for making this investigation possible; and to those nurses and nurses' aids who, by their vigilance, have made it successful.

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CONGENITAL MALFORMATIONS OF THE EYE INDUCED IN MICE BY MATERNAL ANOXIA*

With particular reference to the problem of retrolental fibroplasia in man

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Epidemiologic and clinical evidence has been published which indicates that retrolental fibroplasia, although developing after birth, is basically the equivalent of a congenital defect of the human fetus.[1] The concept is paradoxical in that a congenital anomaly by definition should be present at birth.

In explanation is the fact that retrolental fibroplasia is a disease of prematurity—a borderline period of development when the baby is no less a fetus simply because it is not contained by its mother.[2] Because of relationships of the condition to placenta previa, antepartum hemorrhage, and eclampsia, the hypotheses were advanced that the condition is acquired in the late prenatal or paranatal period of its life and that sublethal anoxia is a principal causative agent.[1-3] Subsequently, the problem was brought into the laboratory[4] as part of a broad investigation of the effects of anoxia on the offspring of pregnant mice.

Following exposure of pregnant mice to rarefied atmospheres, a variety of malformations were observed to develop in both skeletal and soft tissues of the fetus. The experimental epidemiology of these anomalies,

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which include anencephaly, cleft palate, and osseous deformities, has been the subject of study by Ingalls, Curley, and Prindle.[4]

The present report, concerned with developmental anomalies of the eyelids and intraocular structures, adds morphologic analysis to the epidemiologic data in an attempt to gain a better understanding of the genesis and meaning of these defects. With the understanding that the palpebral defect is merely one manifestation of a more complex ocular disorder the whole process is referred to as "open eye."

Review of literature

The generic anomaly classed as open eye is indistinguishable from similar ocular disorders observed by previous investigators.[5] Some of these disorders occurred spontaneously in strains of breeding animals; others were induced under experimental conditions.

Loeffler[6] described open eye of newborn mice as a genetic recessive trait. Either one eye or both eyes were found to be affected but they were not submitted to microscopic study. The opening between the lids varied from pinpoint thinness to wide, and a bloody exudate was present between the lids, resulting in the formation of a scab in the palpebral fissure. Hematoma, especially at the lower lid, was also seen to occur. Eyes affected at birth either recovered or developed persistent corneal cloudiness or opacity with microphthalmia or phthisis bulbi.

A simular, if not identical, anomaly was observed by Strong[7] in newborn mice of his "L" stock. The defect was first manifest as a round opening between the lids; later there developed opacity of the lens associated with diminution in the size of the eyeball. Occasionally, permanent closure of the eyelids was observed with either microphthalmia or marked distortion of the globe. The condition was not studied microscopically.

Reed[8] noticed open eye frequently associated with harelip in a stock of Bagg albino mice. It is said that one or both eyes were open at birth but no histologic details were given.

Gruneberg,[9] studying the development of some external features of the mouse embryo, observed premature opening of the eyelids in one of 26 fetuses examined. The isolated finding was interpreted as pathologic, but it was not investigated histologically.

Following radiation of two female mice, Little and Bagg[10, 11] reported the occurrence of open eye in third- and fourth-generation offspring. The defect was found bilaterally in 81 embryos and unilaterally in 531 embryos with about equal distribution between right and left eye. The space between the eyelids varied from a thin strip to a larger opening resulting from complete absence of the lids.

As in Loeffler's "L" stock, hemorrhagic exudate was frequently noticed both in the lids and in the palpebral fissure with later formation of a scab. The defective eyelid at times was the only ocular finding; at other times there was concurrent deformity of the lens, intraocular hemorrhage, and partial collapse of the retina.

The hemorrhagic change extended occasionally to involve face, mouth, nose, ear, and cerebrum. The external ear occasionally showed evidence of ipsilateral arrested development with deformity of the skull and twisting toward the eye lesion. Likewise associated anomalies of the limbs were not uncommon; they were usually ipsilateral with the eye lesion, rarely contralateral, and consisted mainly of club foot.[12]

Bagg and Little interpreted the ocular anomaly as resulting from a gene mutation produced by radiation. No alternative explanation was considered although Gruneberg later pointed out that, if the mutation was caused by X rays, one would have to assume that precisely the same mutational step—and no others—happened twice independently, a very unlikely event.

Two years after the eye anomaly was described, Bagg and Little[11] demonstrated as-

sociated formations of subcutaneous blebs and hemorrhages. They postulated a relation between "the presence of a defective blood vascular system in the embryos and the later arrested development of the abnormal eyes."

Shortly thereafter Bonnevie advanced the interpretation that such blebs resulted from excessive production of cerebrospinal fluid escaping from the myelencephalon through a transient opening known as the foramen anterius.[13] Whether this is another way of interpreting manifestations of hydrocephalus is not clear.

Plagens,[14] studying a special strain of deformed, X-rayed mice, showed presence of thrombosed vessels in proximity to blebs and hematomas. He inferred that thrombosis and hypoplasia of blood vessels accounted for the extravasations of plasma and red blood cells.

Again under experimental conditions, Warkany and Schraffenberger[15] showed premature opening of the eyelids, in association with more frequent skeletal anomalies, in the offspring of female rats, maintained on a riboflavin-deficient diet during pregnancy. They further demonstrated the occurrence of a similar eye defect in the offspring of female rats kept on a diet deficient in vitamin A.[16]

In addition to the eyelid anomaly, they observed and described a variety of other disorders in intraocular structures: formation of retrolenticular fibrous membrane; failure of development of the conjunctival space; rudimentary cornea and iris; folding, swelling, and disorderly development of the retina, coloboma; lack of development of the vitreous; and frequent hemorrhages in the cavity of the optic vesicle, in the retina, and in the palpebral fissure.

There coexisted other defects in the body such as ectopy of ureteral opening, diaphragmatic hernia, horseshoe and fused kidney, undilated renal pelvis, persistence of both sets of genital ducts, anomalies of the aortic arch, defective interventricular septum, hypospadias, agenesis of one lung, and tracheoesophageal fistula.

Wilson and Barch,[17] under comparable experimental conditions, confirmed these findings; abnormalities of the lids, folding and eversion of the retina, presence of a mass of fibrous connective tissue in the reduced vitreous chamber, persistence of the choroidal fissure, and defects of the ciliary body were also encountered, together with edema of the head, neck, and thorax and hemorrhage in the region of the eye. Similar intraocular anomalies, apparently without gross palpebral defects, have been produced by Gillman and his colleagues[18] by injecting rats with trypan blue at fortnightly intervals before and during pregnancy.

Materials and Methods

Information on the experimental procedure used for production of open eye has been given previously.[4] Briefly it consisted of exposing pregnant mice to less than normal atmospheric pressures in a chamber from which air was continuously being exhausted by a vacuum pump. Entrance of air was restricted by means of an adjustable globe valve and the insertion of a water bottle in the system served to standardize the humidity and temperature of the air.

The animals used in the experiment were white female mice from a strain maintained for about five years in the laboratories of the Department of Epidemiology of the Harvard School of Public Health. A total of 510 pregnant animals, equally divided into three groups, were used in the experiment.

Animals of one group (Group A) were exposed at differing stages of gestation to an atmospheric equivalent of an altitude approximating 27,000 feet (260 mm. Hg); animals of another group (Group B) were similarly exposed but at negative pressures comparable to 25,000 feet (280 mm. Hg); a third group (Group C) was kept as a control and maintained at sea level (760 mm. Hg).

The duration of the exposure in the high altitude chamber was five hours at a temperature of 23 to 25°C. in both experimental groups. The time for decompression and recompression was about 15 minutes in each case, a time judged sufficient to avoid bends.

In order to study the effects of the anoxic insult at successive stages of gestation, the 170 animals of each experimental group (Groups A and B) were subdivided into 17 subgroups of 10 animals. The members of each subgroup in succession from the first to the 17th day of pregnancy received the anoxic insult on one occasion only. The appearance of the copulation plug was considered as indicative of the first day of pregnancy and the contents of the uterus were delivered by surgical section on the 18th day of the gestation period.

The ocular defect was studied in serial, coronal, or tangential sections, six microns thick, of the entire head of the embryo. Paraffin imbedding and hematoxylin and eosin staining were found adequate for a satisfactory microscopic study. Deviations from the normal sequences of development were carefully evaluated by comparison with corresponding structures of litter mates and control embryos of the same age.

Results

Under the given experimental conditions open eye occurred in 10 animals: four times among the animals of Group A, four times among the animals of Group B and twice in Group C among control animals. The experimental procedure, the day of gestation at the time of exposure to the insult, and the site of the eye defect are shown in Table 1.

TABLE 1

Anoxia and Open Eye

Experimental Procedure	Day of Gestation at Time of Insult	Site of Defect
Altitude 27,000 feet	14	Unilateral, left
	16	Bilateral
	16	Unilateral, right
	17	Unilateral, left
25,000 feet	15	Bilateral
	16	Unilateral, left
	17	Unilateral, left
	5*	Bilateral

* Interpreted as chance occurrence.

The two animals* of the control group with open eye were litter mates; the defect was on the right in one and bilateral in the other animal. Except in this instance, no litter contained more than one affected fetus.

Associated gross defects were seen once in the fetus of a mouse exposed on the 14th day of gestation at 27,000 feet, which displayed, in addition to the open eye, cleft palate and extensive hemorrhagic discoloration of the little toe of the left hind foot. A litter mate showed a similar area of hemorrhagic discoloration on the left foreleg and four other mice in the litter displayed cleft palate.

Morphology of open eye

The external ocular defect that justifies the name of open eye is defective formation or separation of the eyelids, permitting direct inspection of the cornea and globe. Mice are normally born with closed eyelids which usually open from 12 to 14 days after birth, as differentiation of the lids and keratinization of the squamous epithelium at their margins is completed.

Gruneberg,[8] in a study of the development of external features of the mouse embryo, mentions the appearance of the eyelids on the 15th day of gestation, "like smooth spectacles" surrounding the eyes. On the 16th day, in 15 of 21 embryos, he noticed that the eyelids were less widely separated leaving only a relatively narrow segment of the eye uncovered; in two or three instances, however, the lids were nearly as wide open as on the previous day; in the remaining six embryos the palpebral fissure was already closed. On the 17th day the eyelids were uniformly found to be closed with one exception. In one of 26 fetuses examined at this

* Interpreted as chance occurrence.

stage of development, one eye was found to be wide open, a feature that the author interpreted as pathologic.

The ocular anomaly in our material was basically similar in different animals. Behind absent or separated lids the eye appeared to bulge somewhat, though it was judged grossly normal in size and location. No differences were observed between skulls of animals displaying the eye defect and those of normal animals, and the bulb, the cornea, the sclera, and the conjunctiva did not seem to be grossly abnormal on examination.

In two animals the palpebral defect was the only ocular disorder evident; in all the remaining animals additional intraocular anomalies were consistently shown by the study of histologic sections. They are schematically represented in Figure 1, illustrated in Figures 2 through 24, and described in the various legends.

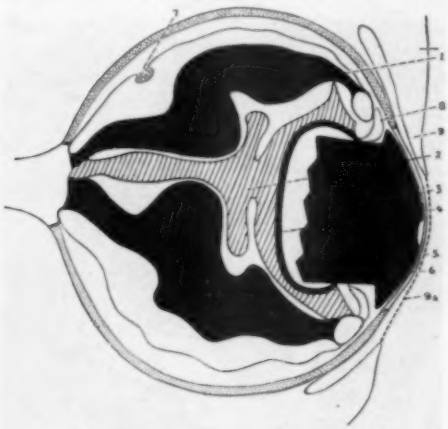

Fig. 1 (Ingalls, Tedeschi, and Helpern). Diagrammatic view of open eye and associated disorders of intraocular structure: (1) Inward folding of the retina. (2) Vasoformative tissue in distorted vitreous. (3) Displacement forward and distortion of the lens with retrogressive change. (4) Detachment and thickening of the hyaline capsule and of the capsula perilenticularis fibrosa. (5) Obliteration of anterior chamber. (6) Atrophy of cornea. (7) Cellular budding in the choroid. (8) Displacement backward of iris. (9) Unjoined eyelids, and (9a) bridge of keratinized squamous epithelium across the cornea connecting the unjoined eyelids.

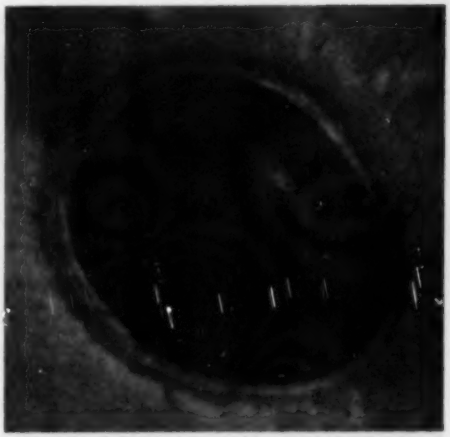

Fig. 2 (Ingalls, Tedeschi, and Helpern). Open eye in the mouse fetus following exposure of the mother to an atmosphere equivalent to 27,000 feet of altitude for five hours on the 17th day of gestation, 260 mm. Hg pressure.

Retina

Under low-power magnifications, the striking finding was that of an inward folding, from moderate to marked, resulting in an undulating structure. At times all the retina was involved; less often the finding was limited to the central or the peripheral portions.

When the retinal folds were cut transversely the cells were radially arranged like the ribs of an open umbrella around a well-defined inner circle, the lumen of the optic vesicle. Whenever there coexisted persistent fetal fissure and the optic cup was penetrated by mesodermal tissue, the resulting pattern was that of a type of coloboma.

According to Lorenz and Dunn,[19] the retina of the normal newborn mouse is composed of four layers; namely, from within outward, a vascular layer, a layer of nerve cells, an inner molecular layer, and an outer undifferentiated layer. These four layers, recognized in the retina of our control series also, could not be made out clearly in the embryos with open eye. Each layer showed frequent variations in thickness, poor cellular differentiation, and frequent intermixing of cells of adjacent layers.

Fig. 3 (Ingalls, Tedeschi, and Helpern). Horizontal section of the head of a mouse embryo with open eye on the right. The inward folding of the retina, the distortion of the lens, and the bridge of vasoformative tissue between the two structures are clearly visible. Notice the concomitant, homolateral, external, and internal hydrocephalus. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

An additional deviation from the normal was contributed by a disorder in vascularity. The thin-walled blood channels of the inner vascular layer were unduly engorged and irregularly distributed, so as to push aside retinal tissue. These blood channels showed marked budding and even more rudimentary vascular structures which at times extended forward into the vitreous, reaching the posterior aspect of the lens.

Shadows of extravasated red cells and abundant amorphous or granular eosinophilic material, the latter suggesting edema, were frequently seen in between both the dilated blood channels and the disorderly aligned retinal cells.

Vitreous

The vitreous was markedly reduced in size and irregular in shape. The most frequent distortion resulted from a narrowing of the central portion with expansion at the sides, in butterflylike configuration. The ground substance varied from granular or fibrillar to a compact structure, but even in the compact areas large vacuoles of various sizes and shapes were noticeable. In some instances the vitreous was reduced to a thin layer of substance so that the inner vascular layer of the retina had become in close contact with the posterior aspect of the lens.

Remnants of the retrolental portion of the hyaloid artery were present. In some ininstances they were present as regularly aligned and evenly interspaced blood channels, in rosarylike fashion along the course of the posterior surface of the lens. In some other instances, blood channels, either sparse or in small clusters, were visible in the bulk

Fig. 4 (Ingalls, Tedeschi, and Helpern). Inward folding of the retina in mouse embryo with palpebral defect. Notice remnants of the hyaloid vascular system behind the distorted lens. Irregularities of contour of the sclera and choroid are also shown. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

of the vitreous itself and they seemed to follow the course of the hyaloid artery.

More often the retrolental vascularity was abnormal as revealed by excessively abundant and disorderly distributed blood channels, displaying marked variations in the size of the lumina. The endothelium lining these channels ranged in shape from flattened to rounded, with a tendency to irregular alignment.

These newly formed blood channels lay in an embryonal type of connective tissue which consisted of an eosinophilic, bright-stained, either compact or vacuolated ground substance in which numerous spindle-shaped, oval, stellate, polyhedral, or irregularly rounded cells were present. Cells with large nuclei, provided with nucleoli, were frequently seen and mitotic figures were counted, as many as five in a field at high magnification.

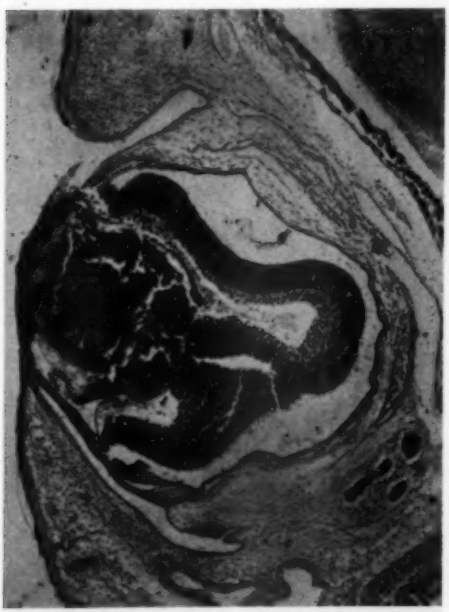

Fig. 5 (Ingalls, Tedeschi, and Helpern). Retinal folds showing variations in thickness and intermixing of cells of adjacent layers. There is coexistent palpebral defect. Photomicrograph 15th day of pregnancy, 260 mm. Hg pressure.

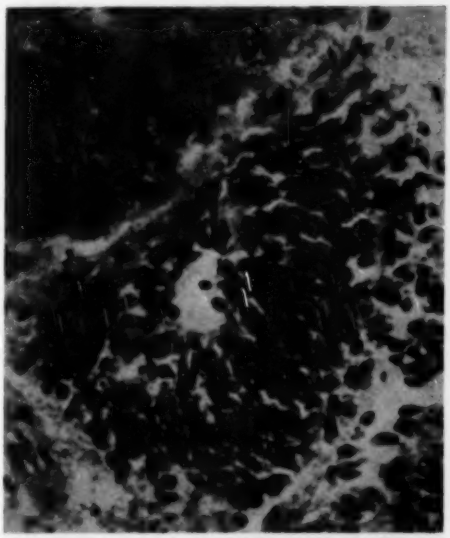

Fig. 6 (Ingalls, Tedeschi, and Helpern). Cross section of retinal fold showing "rosette"-like pattern. Notice the disorganized structure of the retinal layers and the presence of edema and amorphous debris in the surrounding area. Photomicrograph 15th day of pregnancy, 280 mm. Hg pressure.

This vasoformative mesodermal tissue was most abundant in the central portion of the posterior aspect of the lens and it extended toward the infolding retina, often gaining direct contact with the blood channels of the inner portion of the retina. There coexisted shadows of red cells and a scattering of free basophilic granules which most likely represented debris of degenerated cellular structures.

Lens

The distortion of the vitreous was accompanied by an even more pronounced distortion of the lens which was displaced forward in contact with the posterior surface of the cornea. Some of the lens had assumed a roughly squared shape, but the most frequent distortion resulted from a flaring outward of the anterior portion, toward the margin of the optic cup.

Except in the area where the lens had gained contact with the cornea, the hyaline

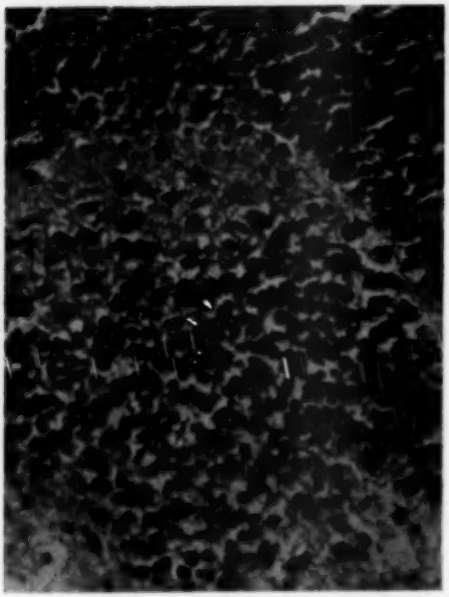

Fig. 7 (Ingalls, Tedeschi, and Helpern). Cellular disorganization in the nerve-cell retinal layer and in the molecular layer with variations in width of both. Photomicrograph 15th day of pregnancy, 280 mm. Hg pressure.

capsule and the capsula perilenticularis fibrosa were completely detached from the lens itself and the resulting space was occupied by fragments of eosinophilic hyaline material and by basophilic granules suggesting debris of degenerated cellular structures. The capsula perilenticularis fibrosa was thicker than normally, due both to the presence of a hyaline ground substance, not seen in the corresponding structure of normal embryos, and to increased cellularity.

These cells showed poorly defined outlines and large nuclei which occupied the greater part of the cell itself. They displayed considerable variation in size, shape, and staining reaction with some appearing darkly stained and others vesicular with occasional patterns suggesting nuclear multilobulation. In some other eyes the fibrous capsule could not be recognized as it had merged with the hyaline capsule of the lens.

The posterior portion of the lens had a ragged margin and it included masses of closely packed cells with poorly preserved nuclear and cytoplasmic structures and frequent cellular debris. Where the equatorial region bulged outward, the cells appeared to be better preserved and more regularly distributed. The anterior epithelial layer was discontinuous in areas and occasionally was completely separated from the main body of the lens by a space filled with retina. Some of these changes were thought to be consistent with early cataract formation.

Iris, ciliary body, choroid, and cornea

The anterior displacement of the lens had resulted in a displacement of the iris and ciliary body which appeared posterior to the equator of the lens rather than anterior to it as in the case of the normal eye. No deviations from the normal were noticed, however, in the intimate structure of either formation.

Fig. 8 (Ingalls, Tedeschi, and Helpern). Atypical bands of vasoformative tissue extending from the retina to the posterior portion of the lens. Notice the intervening edema. Photomicrograph 17th day of pregnancy, 280 mm. Hg pressure.

The sclera, with its attached extrinsic ocular muscles, was clearly made out. It showed occasional swelling by edema and frequently irregularly undulating outline.

The choroid also had lost its usual smooth curvature and although its walls were well preserved, budding of proliferated cells was occasionally observed, a finding not seen in the control series.

The anterior chamber was undeveloped so that the cornea was in direct apposition with the anterior aspect of the lens. The corneal curvature was tortuous, directly following the tortuosities of the distorted lens. The peripheral portions of the cornea were not remarkable but toward the center where it adhered to the lens it was considerably thinned, up to one third of the expected thickness. The various layers could still be recognized, but each layer was reduced in thickness and slightly distorted, presumably from pressure atrophy. The substantia propria seemed to display this pressure atrophy to a greater degree than the other layers.

Fig. 9 (Ingalls, Tedeschi, and Helpern). Vasoformative tissue within the vitreous. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure (see also figs. 10 and 11).

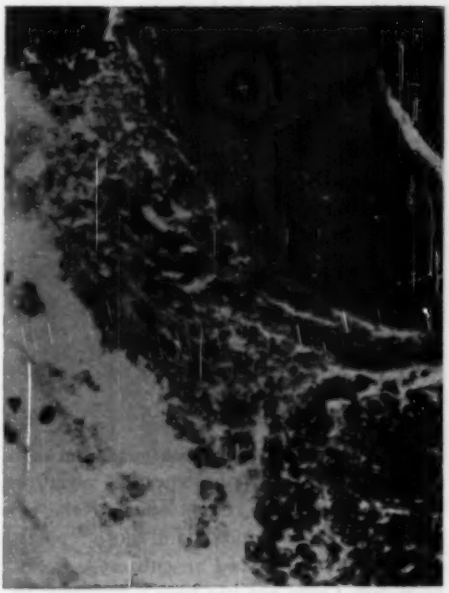

Fig. 10 (Ingalls, Tedeschi, and Helpern). Another pattern formed by vasoformative tissue within the vitreous. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

Palpebrae

Normally the palpebrae in the 18-day mouse embryo are closed and the lines of junction are marked by stratified squamous epithelium. The lids are of uniform thickness and include muscle fibers, hair follicles, and scattered glands which probably represent developing glands of Zeiss. The conjunctiva and the conjunctival space are well developed.

The palpebral defects in animals with open eye varied between two extreme types with many intergrades of deformity discernible. At one extreme the eyelids were completely separated, dwarfed, and with no connection between them. The eyelids had a roughly triangular shape with the apex of the triangle pointing toward the corneal surface. Although stunted, the lids were coated with keratinized, stratified squamous epithelium, and contained hair follicles, glands, and striated muscle fibers.

In some other mice the histologic appear-

ance of the lids was similar except for the presence of a thin bridge of keratinized stratified squamous epithelium connecting the upper and lower margins. This epithelial bridge was in close apposition with the anterior aspect of the cornea and occasionally it was impossible to make out the line of demarcation between the epithelial bridge and the surface epithelium of the cornea. At the other extreme the histologic appearance of the eyelids did not differ from normal except for the fact that they were not joined together as usual.

Discussion

Manifestations of antenatal disease, like those of postnatal disease, are variable. Within the range of expected variation, there is a striking resemblance of the eye defects induced by anoxia and those reported by others who pursued an entirely different approach. Open eye has been previously observed to occur spontaneously in mice and in significant association with harelip, cleft palate, hydrocephalus, and subcutaneous hemorrhages and blebs; under such circumstances the anomaly has been interpreted as a genetic, recessive trait. Furthermore, the defect, or one that is presently indistinguishable from it, has been produced in rodents under experimental conditions through the agency of X rays, vitamin deficiencies, and chemical disturbances during gestation. A dietary deficiency was the underlying injury in the production of the eye defect in Warkany and Schraffenberger's[15,16] and Wilson and Barch's[17] experiments; trypan blue intoxication was the insult employed by Gillman and his colleagues[18] while anoxia was at play in the experiment which led to the development of the eye defect in our own animals.

We interpret these facts to indicate that embryonic susceptibility to the anomaly is revealed under appropriate environmental stress—chemical intoxication, nutritional deficiency, or deprivation of oxygen at a criti-

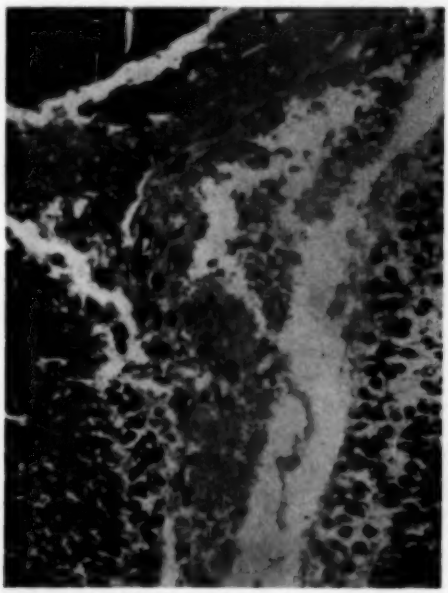

Fig. 11 (Ingalls, Tedeschi, and Helpern). Vasoformative tissue within the vitreous. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

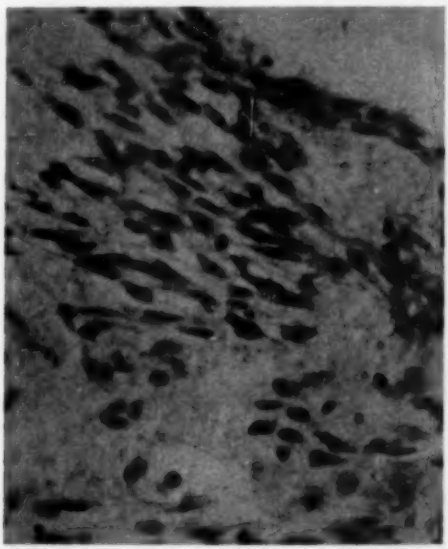

Fig. 12 (Ingalls, Tedeschi, and Helpern). Fibroblastic cell proliferation with poorly developed and disorderly distributed vascular channels behind the lens. Notice the striking mitotic activity. Photomicrograph 17th day of pregnancy, 260 mm. Hg pressure.

Fig. 13 (Ingalls, Tedeschi, and Helpern). Horizontal section of defective eye showing marked distortion of the lens with cataractous change at the posterior aspect and retrolental proliferation of vasoformative tissue. Photomicrographs 16th day of pregnancy, 260 mm. Hg pressure.

Fig. 14 (Ingalls, Tedeschi, and Helpern). Another aspect of distortion of the lens with extensive retrogressive change and detachment of its capsule. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

cal moment of gestation. The importance of timing of the environmental insult is shown by the occurrence of open eye among the progeny of seven of 80 animals rendered anoxic on the 14th through the 17th days of pregnancy. By contrast the defect was observed among the progeny of but one of 260 animals rendered anoxic at other stages of pregnancy and in but one of 170 control litters. Explanation probably lies in Gruneberg's observation that the eyelids are like smooth spectacles surrounding the eyes on the 15th day of development, and are still differentiating the next two days. Experiences with different strains of mice of Loeffler, Strong, Reed, Bagg and Little, Bonnevie,[13] and Plagens[14] suggest that genetic as well as developmental factors determine susceptibility of the embryonic host.

An association is discernible between experimentally produced open eye and other deformities such as cleft palate and hydrocephalus. Although the full meaning of associated anomalies awaits future observations and experiments, the facts to date indicate a necessity to evaluate the roll of the whole organism not merely its parts; the genetic population from which the anomalous individual stems, and of epidemiologic factors acting during pregnancy to produce congenital defects. To assume an anomaly to be inherited just because it is present at birth is unjustifiable. There is need for caution in interpreting Mendelian ratios when the circumstances under which those ratios were obtained are unknown or inadequately defined.

A similar ocular response to entirely different kinds of injurious agents is consistent with two well-established teratogenic principles: namely, unrelated agents acting during pregnancy may give rise to the same type of disorder; and, the resulting anomaly is expectedly a function of the stage of development when the agent is active.[20] The investigation of the stage of development at which an anomaly originates assumes, therefore, as great importance in the search for, causes and control measures as the investigation of genetic factors and nonspecific injurious agents.

Fig. 15 (Ingalls, Tedeschi, and Helpern). Normal lens. The section is technically imperfect at the right upper portion. Photomicrograph of control embryo, 16th day of pregnancy.

Our observations indicate also the need for timing the development of naturally occurring anomalies of the eye and coupling genetic observations with systemic studies of the fetus and its mother in order to clarify relations between the genetic constitution of the host and its intrauterine environment.

For example, some defects of rodents which are primarily attributable to the action of a gene may owe their secondary development to incompatible blood groups as do some defects of human beings. The hemorrhagic phenomenon associated with the naturally occurring and X-ray induced disease, by itself suffices to direct attention on the natural blood groupings of mice and the possibility that erythroblastosislike mechanisms exist.

The ocular changes both in our series and in the comparable series of others are mainly of two types. In one category are ablation, stunting, or distortions of developing tissue —congenital anomalies—that are not observed to arise after differentiation is complete; in the other are retrogressive or productive processes which differ from those to be encountered in postnatal life as a response to injury only in degree and in relation to the greater immaturity of the still undifferentiated cellular elements.

The lack of fusion of the eyelids, the retinal folding, the coloboma and eversion of the retina, the absence of chambers, and the cellular budding in the choroid belong to the group of congenital anomalies. The retrogressive cataractlike changes within the lens and the proliferation of vasoformative tissue, both in the inner vascular layer of the retina and in the retrolental space, are examples of responses not limited to prenatal, juvenile, or adult stages of life.

Numerous gradations were seen of departures from normal development within the two classes of defect. These biologic gradients have been presented schematically

Fig. 16 (Ingalls, Tedeschi, and Helpern). Distorted lens with indistinct conglomeration of cells at its posterior aspect. The capsule is detached and the intervening space is occupied by amorphous, granular material interpreted as cellular debris. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

and photographically. They are interpreted as a manifestation of the variable susceptibility of the whole embryo as well as the eye to the inciting agent—anoxia. The occurrence of the palpebral defect alone, as seen in two of our embryos, is considered a limited and sharply localized ocular response (partial ablation of the lid) to the particular insult occurring on or about the 16th day of embryonic life.

Under the influence of changed environmental conditions, created locally by the present experiment, and on loss of healthy organizing power, the mesenchymal syncytium gives rise to an unbalanced proliferation of vascular elements and supportive fibrocellular stroma, the overall structure being that of an hamartomatous type of growth.

Evidence to support this interpretation

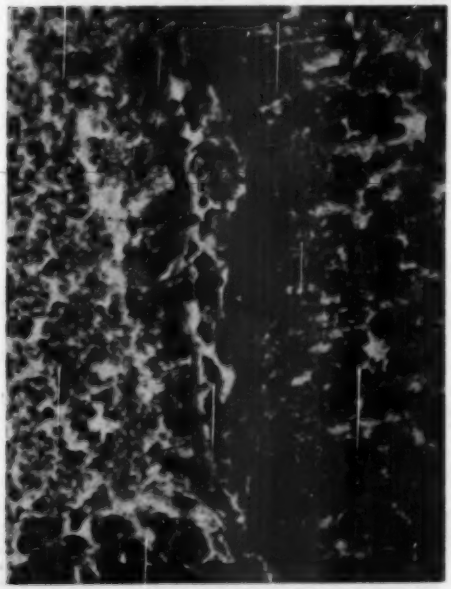

Fig. 17 (Ingalls, Tedeschi, and Helpern). High-power view of same slide as Figure 16, showing retrogressive change of lenticular cells with condensations of elements, and loss of cellular outlines. Notice the marked retrolental edema with cellular shadows suggesting degenerated red cells (see also fig. 18). Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

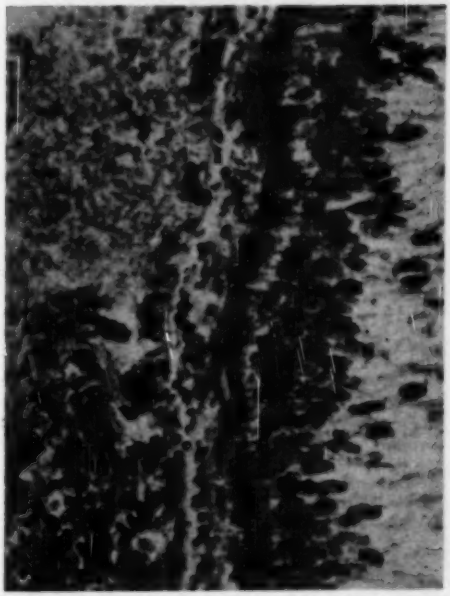

Fig. 18 (Ingalls, Tedeschi, and Helpern). High-power view of same slide as Figure 16, showing abundant scattering of cellular debris between the lens and its detached capsule. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

was found in the excess of mitoses and transitional forms between cells provided with stellate processes, reticulum cells, and flat endothelial cells, forerunners of vascular channels.

Escape of blood elements through these defective channels explains the edema of tissues and hemorrhage so frequently noticed in association with this vasoformative tissue. A similar explanation is offered for the development of the periorbital vascular hamartias noticed in some of our embryos and for the comparable formations described by others elsewhere in the body. The nature of the basic vascular lesion is being studied further.

Open eye and retrolental fibroplasia

Disorders in ocular structure similar to those associated with experimentally produced open eye occur in human beings.

Fig. 19 (Ingalls, Tedeschi, and Helpern). Retinal fold between cataractous lens and its detached anterior capsule. Photomicrograph 16th day of pregnancy, 260 mm. Hg pressure.

Retinal folding, intraocular vasoformative tissue, and disorderly budding of blood channels within the retina are prominent features of retrolental fibroplasia.

The name, retrolental fibroplasia, was introduced by Terry,[21] in 1942, to indicate a condition characterized by the presence of vascular embryonal connective tissue with retinal components behind the lens of the eyes of many prematurely born infants. This name and other descriptive terms used earlier, such as vascular cord in the vitreous, pseudoglioma, persistent hyaloid artery, and congenital retinal folds, reflect the complexity and variety of patterns characterizing the condition.

Terry's hypothesis that retrolental fibroplasia represents a persistence of vascular channels normally present in the premature fetus has been discarded since Owens and Owens[22] have repeatedly observed the condition to develop following normal involution of the hyaloid artery and its capillary branchings.

A modification of Terry's conception of a predisposing (developmental) constitutional factor was advanced by Reese and Payne.[23] They suggested that retrolental fibroplasia was determined by the status of the primary vitreous in the premature fetus, injury being followed by various degrees of hemorrhage, rupture of the lens capsule, glaucoma, and finally by adhesion of the vitreous to the inner surface of the retina. They expressed the belief that the basic process exists before birth and called attention to the frequent association with cutaneous hemangiomas.

Mental retardation, microcephalus or hydrocephalus frequently coexisted in the series of cases reported by Krause[24] and he concluded that retrolental fibroplasia was part of a general systemic process. He

Fig. 20 (Ingalls, Tedeschi, and Helpern). Cellular budding in edematous choroid. Photomicrograph 15th day of pregnancy, 280 mm. Hg pressure.

stressed the need for broader investigation of organs other than the eye.*

After analysis of epidemiologic data presented by Terry, Reese and Payne, and Krause, Ingalls[1] reported three case histories in detail and advanced the suggestions

Fig. 21 (Ingalls, Tedeschi, and Helpern). Anterior portion of the ophthalmic bulb protruding between open eyelids. Notice obliteration of anterior chamber. Photomicrograph 17th day of pregnancy, 280 mm. Hg pressure.

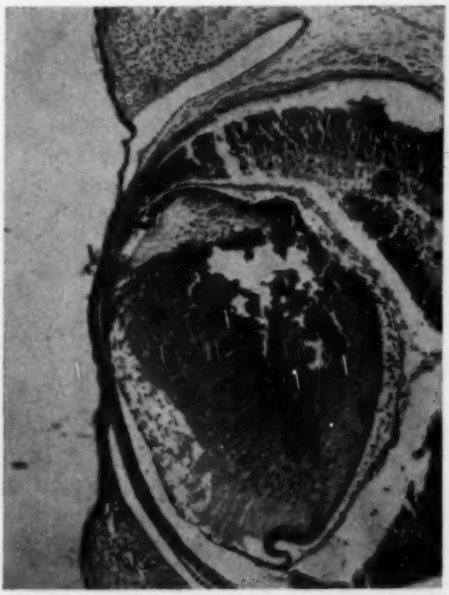

Fig. 22 (Ingalls, Tedeschi, and Helpern). Bridge of squamous keratinized epithelium extending between the eyelids over the cornea. Photomicrograph 17th day of pregnancy, 280 mm. Hg pressure.

that Krause's "pathologic entity" was anoxia; and that anoxia accounted for associations of retrolental fibroplasia with placenta previa, eclampsia, and antepartum hemorrhage. Ingalls also emphasized the distribution of birth weights as indicative of a host factor such as that postulated by Reese and Payne; and as indicating onset of the disease shortly before or around the moment of premature birth.[2,3]

Solid evidence tending to place the genesis of the condition closer and closer to the period of birth has been recently supplied by Guy.[27] Of nearly 300 premature infants examined in the first 10 days of life, 27 had a cloudy vitreous and of these nine subsequently developed retrolental fibroplasia. None of the 244 other premature infants with a clear vitreous during the first 10 days of life developed the condition.

Final proof of the importance of both anoxia and the developmental stage of the fetus

* The suggestion of Krause deserves intensive consideration, for angiomatosis of the retina with associated angiomatous involvement of the brain has been described by Lindau and other workers.[28, 29] Lindau expressed the opinion that these intraocular disorders and the frequently associated vascular anomalies within the brain substance did not represent localized disturbances of the embryonal eye or brain but were part of a broader malformative disorder of the vascular system manifested predominantly but not exclusively within these organs. Of two cases of Lindau's disease studied by Tedeschi,[29] one displayed a variety of vascular hamartias in the brain, lungs, liver, spleen, kidney, and myocardium, and the other in the brain and meninges. These findings confirm and extend Lindau's conception of the systemic nature of this hamartomatous vasoformative process.

Fig. 23 (Ingalls, Tedeschi, and Helpern). Fusion of open eyelid to cornea. Photomicrograph 16th day of pregnancy, 280 mm. Hg pressure.

in the production of retrolental fibroplasia awaits only the confirmation of a recent report by Szewczyk.[28] Nine infants with early signs of retrolental fibroplasia—vascular engorgement and tortuosity, hemorrhages; and beginning retinal detachments—were treated by being placed in an atmosphere of 60 to 70 percent oxygen. There was a dramatic improvement in the ocular disturbances within a day or two. Conversely early changes of the disease were induced in seven premature infants over a period of several days simply by removing them from 50-percent into 22-percent oxygen. The tortuosity of retinal vessels, neovascularization, and beginning retinal separation were rapidly reversed upon exposure to 60-percent oxygen.

If these observations are confirmed, the fragmentary ophthalmologic, obstetric, epidemiologic, and pathologic observations which have been reported to date will find harmonious explanation. The observations of Guy that a cloudy vitreous is a precursor to retrolental fibroplasia fits with Szewczyk's interpretation that "when the oxygen tension in the blood falls below the requirements of the fetal retina, the retinal vessels dilate, then become tortuous and, at the same time, new channels develop. If the demands for oxygen are still not satisfied, edema in the most fetal parts of the retina develops (peripheral gray-white areas). The vessel walls begin to suffer especially at the venous side, because the retina utilizes all the available oxygen, and transudation and hemorrhages take place."

This conception of pathogenesis is also compatible with the sequence of events as described clinically by Owens and Owens,[22] and pathologically by Heath.[29]

Heath's report even though based on histologic specimens—that is to say on tissues from infants sick enough to die or eyes diseased enough to warrant surgical removal—describes early microscopic changes of retrolental fibroplasia. In addition to dilated ves-

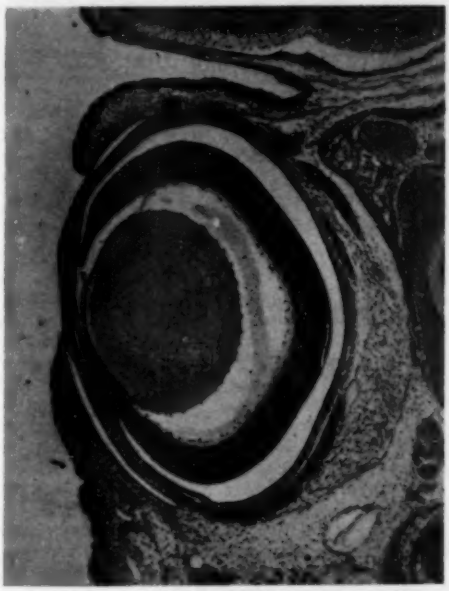

Fig. 24 (Ingalls, Tedeschi, and Helpern). Open eye without any detectable intraocular anomaly. Photomicrograph 16th day of pregnancy, 280 mm. Hg pressure.

sels, edema, hemorrhages, and vascular proliferations on the surface of and within the retina, he observed a delicate haze or cloud of "countless minute, hairlike fibrillae" in the vitreous. . . . When the mistlike fibrillae . . . have developed to the point of organization and the retina is partially separated the process cannot reverse."

Of particular interest in the light of our experimental findings is the general agreement of pathologists on the presence of neovascular, and angiomatous or hamartomatous tissue as a characteristic part of retrolental fibroplasia. First emphasized by Reese and Payne the finding was confirmed by Klien[30] who inferred that retrolental fibroplasia develops from an "angioblastic overgrowth of the primary vitreous in response to some disturbance as yet unknown."

There are but three methods by which to attempt the solution of a medical problem, whether the disturbance be known or unknown. Each method—clinical, epidemiologic, and experimental—has been applied to the problem of retrolental fibroplasia. Strong evidence can now be marshalled from all three avenues of approach to indicate that systemic anoxia is the disturbance that commonly produces retrolental fibroplasia.

In the complex interplay of agent, host, and environment that results in the manifestations of disease, Gordon has time and again stressed the gain to be had by weighing properly the host factor.[31] In the experiments reported here clear evidence was to be had of the importance of the embryonic host in the production of an intraocular defect resembling retrolental fibroplasia. The host factor is interpreted as largely a function of the developmental status of the embryo in general and of the eye in particular at the time when embryonic stress occurs.

The similarities of experimentally produced open eye in rodents to retrolental fibroplasia of human beings are doubly impressive considering the great differences between the two species. Just as the rat has proven a useful animal with which to study rickets, the mouse appears to be a satisfactory species with which to test further the hypothesis that anoxia plays an important role in the etiology of retrolental fibroplasia, and to study the evolution of the basic neovascular lesion. The broad biologic problem involves the whole vascular system with the eye a sensitive barometer of changes taking place elsewhere and with clinical manifestations of anoxia determined by the location of injury.

Summary

During the course of experiments testing the effects of anoxia on the offspring of pregnant mice, congenital anomalies of the fetus characterized by opened eyelids at birth and by associated defects of the retina and vascular system followed anoxic insult on the 16th ±1.5 day of gestation. Extraocular vascular hamartomas and hydrocephalus were also observed in significant association with the ocular anomalies. Since the effects of the anoxic insult were studied in progressive stages of gestation, it was possible to define and analyze developmental features of the embryonic eye that determined the specific ocular anomalies.

Two kinds of defect were observed within the eye. In one category were ablation, stunting, or distortions of developing structures resulting in defects that are not observed to arise after birth—congenital anomalies in short. Secondly, retrogressive or productive processes were seen which differed from those encountered in postnatal life—as a response to injury—only in degree and in relation to the greater immaturity of still undifferentiated cellular elements.

Lack of fusion of the eyelids, retinal folding, coloboma and eversion of the retina, cellular budding in the choroid, and absence of the chambers exemplify the congenital defects; retrogressive changes within the lens and proliferation of vasoformative tissue, both in the inner vascular layer of the retina and in the retrolental space, are examples of responses not limited in respect to

prenatal, juvenile, or adult stages of life. Numerous gradations were seen of deviations from normal structure within the two classes of defect, which are interpreted as a manifestation of the variable susceptibility of the eye to the inciting agent.

The generic anomaly classed as open eye was indistinguishable from similar defects observed by others to occur on a genetic basis in selected strains of naturally born mice; among the third and fourth generation progeny of females exposed to X rays; and among the progeny of animals reared on vitamin-deficient diets or subjected to metabolic injury during pregnancy.

The similar response of the ocular tissues to unrelated injurious agents, the influence of timing of the injury, and genetic constitution of the strain are interpreted as manifestations of the embryonic host in the production of anomalies.

The findings are consistent with two well-established principles of experimental teratology: namely, that unrelated agents acting during pregnancy may give rise to the same type of disorder and that the resulting anomaly is expectedly a function of the stage of development at which the agent is active. Transferred to human epidemiology the findings suggest the importance of time and multiple causative factors as determinants of specific ocular congenital malformations.

There are remarkable similarities of open eye to the retinal vascular disorder, retrolental fibroplasia, so frequently observed among prematurely born babies of late years. Although it is by no means certain that the intraocular lesion of premature babies is the precise counterpart of that condition in the mouse, the possibility seems greatly enhanced by the recent observations of Szewczyk and warrants further consideration.

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RETROLENTAL FIBROPLASIA

A CLINICOPATHOLOGIC STUDY

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Retrolental fibroplasia is a progressive condition usually occurring in premature infants. Essentially, it is a formation of fibrous tissue behind the lens, but the disease is frequently associated with the retinal detachment, retinal folds, glaucoma, microphthalmos, cataract, and corneal opacities. The anterior chamber is very shallow and posterior synechias occur. The iris usually retains its fetal blue color. Nystagmus and strabismus are common.

INCIDENCE

The condition was first described and named by Terry in the United States in 1942, but sporadic cases which resemble the condition have been described since early in the 19th century (Travers, 1820), and toward the close of that century, Treacher Collins (1892) gave a description of the condition in the *Royal London Ophthalmic Hospital Reports.*

The incidence of the disease is interesting. Following Terry's description, large numbers of cases were reported in the United States, but less than a score of cases have been recorded in England (Moffatt, 1950), three cases were reported in Denmark (Holm, 1950), two cases in France (Lelong, Velter, Desvignes, Rossier, and Baron, 1950), one in Spain (Arruga, 1949), and Epstein (1949) asserted the condition was still unknown in South Africa.

Until this series of 23 cases herein reported, no case had been described in Australia. The variability in incidence is seen even in different Australian cities with similar climatic conditions and similar populations, largely of the same race, and similar standards of living and hospital facilities.

TABLE 1

RETROLENTAL FIBROPLASIA CASES AT WOMEN'S HOSPITAL, MELBOURNE

Year	No. Premature Births		No. Cases	% Incidence
1946	50	under 4 lbs. (1,810 gm.)	0	0
1947	50		0	0
1948	36	under 3½ lbs. (1,600 gm.)	7	17
1949	32		6	19
1950	56		8	14
1951 (9 months)	30		0	0

This same variability in distribution was noted in the American cases also.

In Melbourne, during 1948 to 1950, 23 cases occurred, in Tasmania one case, in West Australia none, in South Australia none, and in New South Wales about half a dozen cases. All these places are in the temperate zone and conditions are essentially the same.

This curious localization of the disease extends even to the hospital. In Melbourne, there are two large maternity hospitals, but 21 of the 23 cases come from one of the hospitals, the Women's Hospital.

The number of cases of the disease must be correlated with the number of premature births, and the degree of prematurity of infants surviving long enough to develop the disease. This survival rate will obviously be greater in communities in which there is a skilled care of premature infants. Terry (1945) states that 12 percent of children weighing less than three pounds (1,360 gm.) developed the disease. Crosse (1950) in Birmingham found an incidence of 4.2 percent in premature babies under three pounds. At the Women's Hospital, Melbourne, statistics for the 21 cases are tabulated in Table 1.

In addition there were also two patients born in smaller private hospitals. One was a male born in June, 1949, after 26 weeks' gestation weighing two lb., 12 oz. (2,240 gm.); the other was born after 30 weeks' gestation in May, 1950, weighing two lb., 9 oz. (1,160 gm.). With such small figures reduction to percentage is not very accurate, but, since the first case was seen in 1948, the incidence of the disease in the following three years in babies under 3.5 lbs. (1,600 gm.) is 17 percent.

In the present series the sex incidence is about equal, there being 13 males and 10 females. Runge (1947) reported the disease more common in females. This may be correlated with the greater viability of female infants. In the four years, 1946 to 1950, at the Women's Hospital, Melbourne, 457 stillborn male infants were delivered, compared with 356 stillborn female infants. Bakwin (1946) reported the disease more common in males.

The disease is more common in twins, but

TABLE 2

BIRTH WEIGHTS IN 23 CASES OF RETROLENTAL FIBROPLASIA

Birth Weight	No. Cases
Up to 2 lbs. (906 gm.)	3
2 lbs. 1 oz. (930 gm.)—2 lbs. 8 oz. (1,140 gm.)	4
2 lbs. 9 oz. (1,180 gm.)—3 lbs. (1,360 gm.)	8
3 lbs. 1 oz. (1,390 gm.)—3 lbs. 8 oz. (1,600 gm.)	8

TABLE 3

PERIODS OF GESTATION IN 23 CASES OF RETROLENTAL FIBROPLASIA

Gestation Period	No. Cases
Up to 22 weeks	1
23 weeks–26 weeks	3
27 weeks–30 weeks	14
31 weeks–34 weeks	4
35 weeks–38 weeks	1

in all the three cases reported here one of the twins died within a few hours of birth. It is probably the increased risk of prematurity in twins rather than the fact of twinship alone which causes the greater incidence of retrolental fibroplasia.

The birth weights of the 23 cases are shown in Table 2.

Periods of gestation for the 23 cases are listed in Table 3.

In considering these figures it must be remembered that only babies that have survived long enough to develop the disease are included. However, the incidence of the disease was certainly greater than the few references in the literature suggest. A review of the pathologic material in any large hospital will show cases which are undoubtedly retrolental fibroplasia labelled pseudoglioma or endophthalmitis. It is my opinion that many cases of retinal folds previously thought to be congenital in origin are really healed forms of retrolental fibroplasia.

Investigation

When the first cases were seen at the Women's Hospital, Melbourne, in 1948, it was decided to review all the premature babies weighing less than four lb. (1,810 gm.) at birth, born at the hospital since January, 1946. To this end a questionnaire was sent to the mothers of such babies and the records of the Royal Victorian Institute for the Blind were searched for likely cases. From this questionnaire, cases were selected and recalled for examination. However, no cases, other than those already known, were discovered. In September, 1949, it was decided to examine once a month the fundi of all premature babies under 3.5 lb. (1,600 gm.) and follow up any doubtful cases. Up until September, 1951, 115 babies had been examined.

Delayed retinal coaptation

Examination of the fundi of these premature babies showed that in about half of them, there were peripheral retinal detachments. Some were large but others were small and peripheral. They appeared as greenish-gray elevations in the peripheral retina with dark blood vessels coursing over them. They were first seen in the nasal and temporal quadrants but often the entire circumference was involved. The earliest they have been observed was seven days after birth in an infant born after 27 weeks' gestation and weighing two lb., 10.5 oz. (1,260 gm.). Occasionally they have been seen in full-term infants.

In all cases these fundi have been examined at monthly intervals. It is usually found that the detachment slowly recedes over a period of months and the final picture shows peripheral retinal pigmentation of the "pepper and salt" type. Sometimes the detachment is central and not peripheral. Usually, unless the case is progressing to retrolental fibroplasia, the vitreous remains clear. This observation probably provides the reason for "pepper and salt pigmentation" for which various explanations have been suggested in the past.

An opportunity was afforded to examine these detachments histologically in two infants, in whom the condition had been diagnosed clinically and who died of bronchopneumonia. The eyes were obtained post mortem, were fixed in Zenker's fluid, and celloidin sections were cut and stained with hematoxylin and eosin. Examination of these showed:

Baby R:

This infant, a female, was born on June 23, 1950, after 30 weeks' gestation and weighed two lb., one oz. (930 gm.). Examination of the eyes on July 13, 1950, showed bilateral delayed retinal coaptation. She died on July 16, 1950, and histologic examination of the eyes showed:

Left eye. The cornea is normal and the angle of the anterior chamber is well formed. The canal of Schlemm is present. The retina shows a separation between the pigment layer and the inner layers. The inner layers

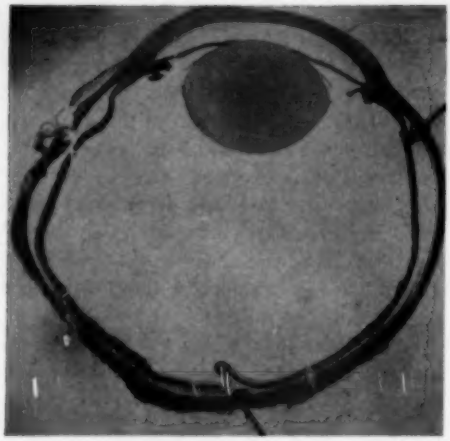

Fig. 1 (Ryan). Baby R. Left eye, showing delayed retinal coaptation. Arrows indicate retinal folds.

are loose on the pigment layer particularly at the ora on one side and toward the posterior pole where a retinal fold is present (fig. 1).

Right eye. The picture is similar to the left eye except that the retinal fold is nearer the ora. Serous fluid separates the two retinal layers. Figure 2 shows the retinal fold.

Fig. 2 (Ryan). Baby R. Right eye, showing retinal fold with subretinal exudate. (×130.)

BABY J.

This infant, a female born on September 2, 1950, after 28 weeks' gestation, weighed three lb., three oz. (1,475 gm.). Examination of the eyes on November 8, 1950, showed marked delayed retinal coaptation. The infant died on December 12, 1950, and both eyes were obtained.

Histologic examination of both eyes shows a looseness of the inner on the outer layer of the retina but, owing to tears in the retina at the region of the ora, it is impossible to be sure the condition is not an artefact (figs. 3 and 4).

The detachment seen is therefore due to a looseness of the inner layer of the optic cup on the outer—the former being too large to fit snugly on the latter.

Ida Mann (1937) writes "since the coaptation of the inner and outer layers of the optic cup is never, even in the adult, an anatomical continuity but merely a superposition, it is to be expected that for a large part of intrauterine life the connection will be very indefinite indeed. For one thing, so long as the eye is increasing in size and altering its shape, the growth rate of the inner layer must differ both in various regions and in relation to that of the outer layer.

"Although finally the exact surface area of the inner side of the retina must be mathematically slightly smaller than that of the pigment epithelium, yet during much of the growth period it is appreciably greater. . . . Therefore we shall not be surprised to see that complete or partial persistence of the cavity of the primary optic vesicle (which is another way of saying that the retina is detached, both developmentally and clinically) is normal in the developing eye. At first the appearance was thought to be an artefact (separation of layers by shrinkage during fixation) but Seefelder and other

embryologists have shown conclusively that this is not so.

"During the early growth periods up to the 3rd month the separation is great. After that the layers often appear in apposition but separation occurs very easily, especially in the less differentiated anterior parts (with the exception of the ciliary epithelium where the adhesion of the two layers to each other is always very strong)."

The fundal appearance is therefore produced by delay in coaptation of the inner and outer retinal layers. It is obvious that, in an infant born after six to seven months' gestation, a slight disturbance in the developing retina or choroid can very easily lead to the appearance of retinal detachment. Whether the detachment subsides or persists depends on the state of the development of the eye, the duration for which a noxious influence may act, the strength of the noxious agent, and the resistance of the patient.

In a large percentage of cases, in fact the majority, the detachment subsides over a period of many months and the retina develops a peripheral "pepper and salt" pigmentation. But in a few cases, those going on to retrolental fibroplasia, the vitreous becomes hazy and there is sometimes some dilatation of the retinal blood vessels.

The vitreous haze is fine and uniform and usually appears from eight to 16 weeks after birth. It is probably cellular in nature and it may be lymphocytic or more probably fibroblastic. Since lymphocytes are rare in the sections, a primary inflammatory (infective) origin is rendered very unlikely. The "fibroblasts" may however be glial in origin.

The vitreous haze is usually rapidly followed by the appearance of a mass of white tissue growing in from the periphery, the retrolental membrane. This membrane may be complete or partial, and it may be thick and impervious to light or thin and transmit the red fundus reflex. The membrane arises from the pars plana of the ciliary body (fig. 5). Figure 6, a high-power view, shows the membrane arising from the pars plana. It is

Fig. 3 (Ryan). Baby J. Right eye, showing delayed retinal coaptation with folds.

obvious that it is not inflammatory in nature.

The condition may halt at this stage and the retina return to its normal position, leaving the retrolental membrane in situ, as in Case 20. It is my impression that, when the membrane is thin, some resolution of the fibrous tissue can occur and the membrane become more transparent. This statement is impossible to prove since it is impossible to assess accurately the visual acuity of partially blind infants, but the impression is

Fig. 4 (Ryan). Baby J. Left eye, showing delayed retinal coaptation.

Fig. 5 (Ryan). Case 8. Right eye. Retrolental fibroplasia. Arrow shows origin of retrolental membrane from pars plana of ciliary body.

based on clinical observations over three years.

The retina when it has become replaced may appear normal (Case 20), but more frequently the fundus is white and shows masses of cholesterol crystals and pigmentation (Case 1). The vision remaining in the eye depends on the thickness of the membrane, its site and extent, and the condition of the retina behind. Even with moderately gross lesions, reasonable vision is possible.

Frequently the retinal detachment continues to increase in size and the two folds meet behind the lens to form an umbrella detachment (fig. 7), but the retrolental membrane is not formed by fusion of the anterior folds of the retinal detachment as some assert (Owens and Owens, 1948).

Figure 5 (Case 8) shows the retrolental membrane complete, while the retinal detachment is still separated from it by a wide expanse of vitreous. The eye is now permanently blind and the following changes occur: the anterior chamber becomes very shallow in its center but remains deep at the periphery (fig. 7).

This is the arrangement during the last months of development and is perpetuated by the contraction of the fibrous tissue of the retrolental membrane forcing the lens still further forward. Sometimes, however, the iris becomes adherent to the cornea at the periphery and the angle may be blocked so that glaucoma supervenes.

The iris and lens may come in contact with the cornea and produce corneal opacities and cataract. Occasionally the iris retracts so that the processes of the ciliary body appear stretching toward the periphery of the lens. This has not been observed so frequently as reported by others—it has been seen in only one case.

Nystagmus which may be rotary or searching and convergent strabismus occur. The final stage is a soft shrunken eye. It may be noted that in two cases the iris developed brown pigmentation. This also points away from any inflammatory origin since it repre-

Fig. 6 (Ryan). Case 8. Right eye. Retrolental fibroplasia, showing origin of membrane from clear cells of the pars plana. (×275).

sents an attempted normal stage of development of the mesoderm.

ETIOLOGY

Extensive investigations into the etiology of the disease have been carried out in America by Krause (1946) and others. Krause investigated his cases from the point of view of heredity, family environment, age of parents, time of conception and birth, parity, multiple births, sex of the infant affected, race, maternal disease, and neonatal clinical symptoms, such as cyanosis, jaundice, and asphyxia, and congenital anomalies. However, no factor seemed significant except perhaps maternal bleeding during pregnancy. This however is more likely to be the cause of the prematurity itself.

The cases here reported were reviewed from the aspect of parity, anomalies of previous pregnancies (for example, miscarriage), previous premature infants, any illness or unusual feature during pregnancy (for example, hemorrhage or hypertension), mother's condition immediately prior to delivery, the cause of the premature labor, period of gestation, and the date of birth.

The actual labor was considered in respect to length of labor, time of rupture of the membranes, the nature of delivery (for example, breach or vertex), and anesthetic used.

The postnatal period was investigated regarding resuscitation required by the baby after delivery, the baby's general condition at birth and in the early neonatal period, the occurrence of cyanotic attacks, any blood transfusions required, and any therapeutic measures used such as thyroid, stilbestrol, vitamin E, penicillin, streptomycin, and neptal. The infant's general progress was also noted.

Consideration of all these factors showed nothing significant and, in this respect, my investigations are in agreement with others who have looked to similar factors for the causation of the disease. At one stage, it was thought that light shining in the premature infant's eye might have been a factor in producing the disease, but covering the eyes of all infants had no effect on the incidence.

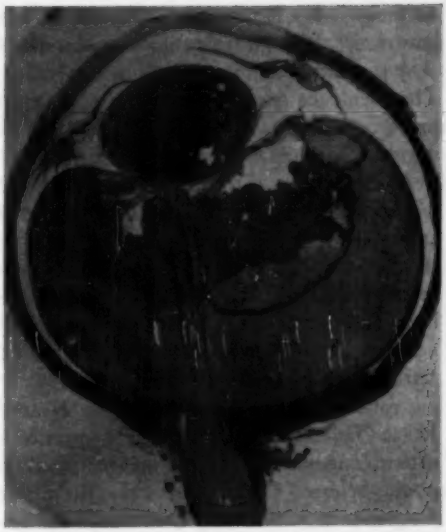

Fig. 7 (Ryan). Case 9. Left eye. Retrolental fibroplasia, showing umbrella detachment.

From December, 1949, all infants under 3.5 lb. (1,600 gm.) at birth were given 150 mg. of vitamin E (a-tocopherol acetate) a day. But between that time and October, 1950, when the drug was discontinued, nine cases of the disease occurred. These cases appeared just as severe as any previous case and the drug gave no evidence of being of value.

It was, however, noted that no case of retrolental fibroplasia had occurred at the Women's Hospital prior to the introduction of a most efficient oxygen cot. With this apparatus it was the practice of the nursing staff to give oxygen liberally to all babies, even when apparently not requiring it.

For these reasons, slender though they were, it was decided in October, 1950, to restrict the use of oxygen to those babies that were actually cyanosed. Since that date no

further case of retrolental fibroplasia has occurred, although there have been many very premature and very small babies reared. The incidence of delayed retinal coaptation has shown no alteration. These facts may be purely coincidental or perhaps significant.

As far as it can be ascertained, there are no figures giving the incidence of congenital anomalies in premature infants. However, in these 23 babies there was one case of hydrocephalus, one of congenital dislocation of the hips, and one of congenital heart disease.

Minton (1951) in describing two cases of retrolental fibroplasia mentions one as having multiple congenital deformities. Krause (1946) believes the condition to be part of a wider congenital encephalo-ophthalmic dysplasia. Scobee (1951) showed that there was a significant relationship between prematurity and strabismus.

Pathology

It has been possible to obtain and section three eyes from two cases of the disease. Two of the eyes were obtained from an infant (Case 8) who died three months after the onset of the disease and one was excised four and one-half months after the onset (Case 9). All the eyes were fixed in Zenker's solution prior to celloidin embedding, cutting, and staining with hematoxylin and eosin.

Baby L. (Case 8)

The eyes were removed four hours after death and fixed in Zenker's solution.

Right eye (fig. 5). The eye measures 16 mm. by 16 mm. The cornea is normal. There are no keratic precipitates to be seen on the endothelium. The anterior chamber is very shallow but the angles are open and the pectinate ligament is well marked. The whole of the lens-iris diaphragm has been displaced forward. Schlemm's canal is well formed.

The iris is cellular, as is normal in infants' eyes, and shows a few lymphocytes. The pupil which is small (one mm. in diameter) is occluded by a connective tissue membrane and the iris is adherent to the lens capsule for one mm. around the pupil margin. The iris shows a tendency to iris bombé.

The lens is normal in shape and the suspensory ligament is well marked. Behind the lens is a diaphragm of connective tissue more marked to one side.

On this side it is composed of long spindle-shaped cells running from the pars plana of the ciliary body toward the posterior surface of the lens. Into it can be seen marked proliferation of the clear cells of the pars plana of the ciliary body. On the less marked side, the diaphragm is composed of a few spindle cells only, although the clear cells of the pars plana show proliferation about midway between the ora serrata and the first ciliary process. The proliferation is localized and the clear cells form a layer five cells thick (fig. 6).

The ciliary body is cellular and shows an occasional lymphocyte and plasma cell, but there are no aggregations of inflammatory cells. The retina is completely detached as far forward as the ora serrata.

Left eye. The eye measures 16 mm. by 16 mm. The cornea is normal but in one area near the center the iris is adherent to it. The anterior chamber is extremely shallow owing to the advancement of the lens-iris diaphragm. The pupil is occluded by a layer of fibrous tissue approximately four cells thick. The angle shows marked pectinate ligaments and Schlemm's canal is present.

The lens is normal but during preparation has split in the anteroposterior axis. There are broad posterior synechias, and a large cyst has formed in the pigment layer of the iris. The iris has the normal cellular appearance of the infantile iris. The ciliary body is also cellular but normal.

Behind the lens is a delicate connective-tissue membrane arising from the pars plana of the ciliary body. In one area it is thickened and contains lymphocytes and endothelial cells. The retina is completely detached on one side as far as the ciliary processes and on the other halfway along the pars

plana, and is bunched behind the lens. The choroid is normal.

BABY M (Case 9)

Left eye (fig. 7). The eye measures 17 mm. by 16 mm. The cornea is normal. The pectinate ligament is very prominent and there are wide spaces between the strands. The iris is cellular and there is a thin strand of fibrous tissue occluding most of the pupil. The iris is adherent to the lens in the anterior portion. The lens is normal.

The tissues of the ciliary body are edematous, and there is marked proliferation of the clear cells to form a cyclitic membrane. This membrane is thick and, in its central portion, acellular, except for a few small round cells. The choroid is cellular but normal.

The retina is completely detached and bunched in a mass behind the lens, while the optic nerve has been dragged into the globe. The vitreous shows a few large irregularly shaped cells.

COMMENT

These slides confirm, in the main, Wolff's (1950) opinion and there seems no doubt that the retrolental membrane is a cyclitic membrane. In none of the three eyes, however, does the detachment extend far along the pars plana. So in these cases it may be supposed that the retinal detachment commenced after the third or fourth month of intrauterine life since after that time the clear and pigment cell layers are firmly united.

The cells found in the cyclitic membrane are mainly fibroblasts and there are a few lymphocytes and endothelial cells. Polymorphs are absent and the condition seems to be one akin to that seen to follow longstanding detachments of the retina in adults.

Delay in retinal coaptation (which is a form of retinal detachment) has been found to occur in approximately 50 percent of premature babies; however, in all but 17 percent of babies weighing 3.5 lb. (1,600 gm.) or less at birth it clears up without serious results. For some reason, of which we are still ignorant, in 17 percent it goes on to produce retrolental fibroplasia.

Not only is the cause of retrolental fibroplasia obscure, but the nature of the condition is still in dispute. Terry (1943) considered it congenital, Wolff (1950) thought it inflammatory, Klien (1949) was of the opinion that it was neoplastic, and Reese and Blodi (1951) suggested it had some relation to adrenal function.

It would appear that a rational explanation of its origin must take into account the following facts:

1. Certain features of the condition are normal in fetuses of 24 to 36 weeks, namely: (a) Looseness of the inner layer of the optic cup on the outer; (b) dilatation of retinal and choroidal blood vessels (See Figure 170, Mann: *Development of the Human Eye.* 2nd edition); (c) anterior chamber deep in the periphery and shallow in the center; (d) presence of remains of glial and angioblastic tissue of fetal intraocular blood system.

2. Pure arrests of development are rare at any stage but practically all developmental anomalies arise as an arrest to which is added a superimposed aberration of development, extended in time and probably representing an attempted adjustment of adjacent parts to each other after the dislocation caused by the initial arrest. (Thus, as was shown long ago by von Szily, both coloboma of the choroid and orbital retinal cysts can be followed experimentally over a period of a week or more in rabbits, during which time the developing abnormality follows a definite course of abnormal growth ending in the finished clinical entity at birth.)

3. The normal human fetus in utero is always cyanosed since, owing to the peculiarities of the placental circulation, none of the arteries carry pure arterial blood. Even the oxygen content of the blood in the umbilical vein is lower than that of the maternal arterial blood. Since high oxygen concentrations are toxic to adults it is possible that

even "normal" concentrations are toxic to immature tissues.

In view of these points it seems possible that retrolental fibroplasia can be considered as an arrest of intraocular development at the moment of or soon after birth (premature) followed by an abnormal aberrant growth largely "compensatory."

The toxic agent may well be oxygen, as suggested by Dr. Kate Campbell, either, doubtfully, in the ordinary inspired air, or, more likely, in the air of an oxygen tent. Some effects of the heightened metabolism could well be stimulation of mitosis, hence overgrowth of glial and fibrous tissue, increase of vascularity, and increased growth rate of the inner layer of the optic cup leading to further detachment. The predisposing factors (delayed retinal coaptation, dilated blood vessels, and glial and fibroblastic remnants) are bound to be present in all prematures of 24 to 36 weeks.

Thus we may be witnessing clinically the developing stages of an anomaly, rather than the results of infection, heredity, deficiency, or metabolic disease as various observers have suggested.

The prematurity provides the initial arrest of development and the administration of excess oxygen, by providing a more or less continuously abnormal environment, stimulates the superimposed aberrant development.

It is also likely that this affords an explanation of Krause's findings of coincidental abnormalities of the central nervous system, since similar arrest and aberrance could occur in any tissue or organ which has not reached full differentiation at the time of the premature birth.

Case histories

No accurate records have been kept of the amount of oxygen given to each child, but all the children in the following case histories who were born at the Women's Hospital were kept for a week or more in an oxygen cot in which the percentage of oxygen was between 40 and 60. Oxygen was given very liberally with the object of preventing any cyanosis developing rather than for treating cyanosis.

Case 1

Baby D. B. This female child was one of twins born at the Women's Hospital, Melbourne, on August 29, 1949. The other child failed to survive. The birth weight was two lb. 10 oz. (1,200 gm.) and the child was born after 32 weeks of pregnancy.

When seen for the first time on December 9, 1949, the right fundus showed large gray masses peripherally, and the left eye showed gray masses above and laterally and some dilation of the retinal veins.

Ten days later a-tocopherol acetate (50 mg., twice daily) was commenced. On January 13, 1950, the right retina was almost completely detached except centrally while the left eye was completely detached and there was a retinal fold running from the 12-o'clock position to the 4-o'clock. There was a posterior synechia at the 4-o'clock position.

By February 10, 1950, the anterior chamber was shallow particularly in the left eye, but otherwise the signs were unchanged. On April 14, 1950, the retrolental membrane was complete in the right eye and, in the left fundus, the retina was returning to position and showed large white masses and shining crystals. The fold was still present.

The right eye remained unchanged but the condition in the left eye slowly subsided so that by September 8, 1950, a good view of the replaced retina was obtainable. It showed crystals, white areas, and pigmentation. The child, when seen on January 12, 1951, appeared to have no perception of light in either eye (would not fix a light) and had nystagmus.

When seen on April 14, 1951, the mother reported that she thought the child, now aged 20 months, could see large objects. It was noted that the iris in both eyes was brown, the right eye had a complete retrolental membrane. The fundus of the left eye had a massive white area with many glistening crystals over the whole temporal half. The nasal half appeared normal. Behind the lens on the temporal side there was a thick retrolental membrane corresponding in position to the damaged retina.

Case 2

Baby B. This male child was born at the Women's Hospital, Melbourne, on May 14, 1950, at the 29th week of gestation and weighed two lb. 8 oz. (1,150 gm.). For three days after birth it suffered from melena, and, six weeks after birth since its hemoglobin was 56 percent, a transfusion was given. A fortnight after birth, vitamin E (150 mg., per day) was commenced. On July 7, 1950, it developed an upper respiratory tract infection for which streptomycin and aureomycin were given.

The eye was first examined on July 14, 1950, when a peripheral gray detachment was noted in the right eye. The left eye was normal. On August 11, 1950, the blood vessels were noted to be greatly dilated and there were large gray retinal detachments in both eyes. The left eye showed early formation of a retrolental membrane.

One month later there was a complete retrolental mass in both eyes, but it was thinner in the center so that a central red reflex could be obtained.

The right eye, when examined one month later, showed a widely dilated pupil which exposed the ciliary processes as described by Terry. The left eye still showed a membrane which was thinner in the center.

A fortnight later the right eye developed an acute rise in tension but responded to intensive eserine therapy. No further change was seen when the infant was last examined on February 9, 1951.

CASE 3

Baby R. B. This female infant was born at the Women's Hospital, Melbourne, on January 19, 1949, at the 22nd week of gestation and weighed one lb., 7 oz. (700 gm.). It was not examined until December 9, 1949, when the left eye was found to have a complete retrolental membrane. The right eye was normal.

CASE 4

Baby M. C. This male infant was born at a small private hospital, and immediately transferred to a Children's Hospital in Melbourne, on June 2, 1949, after 26 weeks of gestation and weighed two lb. 12 oz. (1,270 gm.). It was one of twins but the other twin died soon after delivery. Because the child would not follow a light it was examined under general anesthesia on December 1, 1949.

The right fundus showed an atrophic retina with patches of pigmentation. The disc was very pale and had a sharp medial edge, while the blood vessels were confined to the temporal edge and entered around the edge of the disc. The diagnosis made was that of ectasia of the disc. The eye was blind.

The left eye showed a fine retrolental membrane, through which a faint red reflex was obtainable, through the lower half which appeared thinner than the rest. There were some thin blood vessels on the membrane. There was persistence of the pupillary membrane over a fanlike area in the upper nasal quadrant. The left lens was needled by Dr. A. S. Anderson on December 28, 1949, but the lens did not absorb. The eye was blind.

CASE 5

Baby P. G. This male child was born at the Women's Hospital, Melbourne, June 1, 1949, at the 30th week of gestation and weighed two lb. 9 oz. (1,160 gm.). It was one of twins, but the second twin died 32 hours after birth. Since it seemed possible that he would develop retrolental fibroplasia, his eyes were protected from light. When examined on October 4, 1949, there were complete retrolental membranes and nystagmus in each eye.

CASE 6

Baby B. H. This female infant was born at the Women's Hospital, Melbourne, December 17, 1948, after 32 weeks gestation and weighed three lb. 7 oz. (1,570 gm.). One month after birth it developed fever for which it was given penicillin, sulfanilamide, and oxygen. On May 5, 1951, it could only see light. The right eye shows a complete retrolental membrane and in the temporal half of the left eye, the retrolental space is covered by membrane.

CASE 7

Baby H. This female child was born at the Women's Hospital, Melbourne, on March 6, 1950, at 22 weeks' gestation and weighed two lb. 2 oz. (960 gm.)

When examined on July 14, 1950, the right eye showed a large strand of fibrous tissue anteriorly behind the lens connecting with a retinal fold which ran back to the disc posteriorly. It was situated in the 9-o'clock position on the retina and just below it was a small vitreous hemorrhage. The left eye showed large gray masses below.

The infant was examined at monthly intervals. When last examined on April 13, 1951, the right fundus showed a white patch of atrophy just above the macula and a fold of retina in the 9-o'clock position running from the disc toward the retrolental space where is a connective-tissue membrane spread over the lens from the 9-o'clock to the 7-o'clock meridian. The left eye showed the retina back in place. Both eyes were myopic.

CASE 8

Baby L. This female infant was born at the Women's Hospital, Melbourne, July 14, 1950, and died on December 20, 1950. Both eyes were obtained after death (fig. 5, right eye). The birth weight was two lb. 11 oz. (1,230 gm.) and the gestation period was 28 weeks. A week after birth she developed pneumonia for which she was given penicillin, and a week later a transfusion was given. By July 13, 1950, hydrocephalus was obvious.

The eyes were first examined on August 30, 1950, six weeks after birth. In both eyes large gray masses were visible above.

Six weeks later there were large masses in the right peripheral fundus and the vitreous was hazy. The left eye showed a complete retrolental membrane. At this time the circumference of the head was 16 inches (40 cm.).

Ultimately both anterior chambers became very shallow and a complete membrane had formed behind each lens before death. A full post-mortem examination was not performed so that the cause of the hydrocephalus remains unknown.

CASE 9

Baby M. This male child was born at the Women's Hospital, Melbourne, January 17, 1948, at the 30th week of gestation, and its birth weight was three lb. 3 oz. (1,450 gm.). When seen on May 21, 1948, there was a complete retrolental membrane in the left eye and the eye was excised on June 4, 1948, because of the suspicion of glioma.

The right eye was normal.

CASE 10

Baby L. M. This girl was born at the Women's Hospital, Melbourne, on August 10, 1949, and weighed one lb. 14 oz (850 gm.). It was at the 32nd week of gestation. When seen on September 8, 1950, the cornea of the right eye was opaque and edematous, the anterior chamber was very shallow, and no view of the lens could be obtained. In the left eye there was a complete retrolental membrane. In addition to the above defects the baby also has bilateral congenital dislocation of the hips.

CASE 11

Baby McG. This boy was born at a private hospital in Melbourne, on May 11, 1950, at 30 weeks' gestation, and weighed two lb. 9 oz. (1,160 gm.). He became very edematous immediately after birth. The first eye examination on July 3, 1950, showed, in the right eye, masses nasally and, in the left eye, in the upper nasal and temporal quadrants. From the latter a strand of fibrous tissue ran into the vitreous.

When seen two months later, there was a complete retrolental membrane in each eye. No further change has occurred since, except that the anterior chambers have become very shallow and a fibrous tissue membrane is growing across the pupil.

CASE 12

Baby McK. This female infant was born at the Women's Hospital, Melbourne, on August 2, 1950, weighing two lb. 11 oz. (1,230 gm.), at the 28th week of gestation.

It was first seen on October 13, 1950, but was difficult to examine and no abnormality was seen. However, when seen on November 16, 1950, there was a large retrolental mass and membrane over the nasal side of the right eye and, in the left eye, vitreous opacities were marked.

A fortnight later there was a complete membrane in the right eye and, in the left eye, a mass had appeared below and nasally. On February 20, 1951, there was a complete membrane in each eye and both eyes showed very shallow anterior chambers and synechias.

CASE 13

Baby McC. This male child was born at the Women's Hospital, Melbourne, on October 8, 1948, at 30 weeks' gestation, and weighed three lb. 2 oz. (1,420 gm.). It was not seen by me until March 9, 1951, when it showed a complete membrane in the right eye. The left eye showed a shallow anterior chamber, corneal opacities, and edema. The left pupil was small and the eye shrinking.

CASE 14

Baby McQ. This boy was born at the Women's Hospital, Melbourne, January 16, 1949, at 32 weeks' gestation and weighed three lb. 1.5 oz. (1,410 gm.). It was first seen on March 3, 1951.

The right eye showed a retinal fold running from the disc to the posterior lens capsule, joining there a fine connective-tissue stroma behind the lens. The fold was at the 7-o'clock position. A similar picture was present in the left eye but the fold was at the 4-o'clock position. The child is not blind and is able to distinguish such objects as spoons.

CASE 15

Baby H. N. This female child was born at the Women's Hospital, Melbourne, on May 26, 1948, weighing one lb. 11 oz. (790 gm.) at 28 weeks' gestation. Four months after birth a complete retrolental membrane was present in the left eye and a partial membrane in the right. A year later both eyes showed sudden rise in tension which subsided with intensive eserine treatment. Nine months later the left eye again became glaucomatous but responded to treatment.

CASE 16

Baby P. This female infant was born at the Women's Hospital, Melbourne, and was one of twins born on June 15, 1950. The other twin died soon after birth. The birth weight was two lb. 5 oz. (1,050 gm.), and the period of gestation was 28 weeks.

When three weeks old, it developed pneumonia for which streptomycin and aureomycin were given. On July 27, 1950, it was given a transfusion for anemia and a fortnight later again developed pneumonia for which streptomycin and penicillin were given.

When examined on September 8, 1950, there was a dark mass on the temporal side of the right fundus and a more centrally situated mass in the left fundus. On September 16, 1950, the right eye showed a retrolental membrane and the pupil was bound down with posterior synechias. The left eye showed a similar picture with the addition of corneal edema.

CASE 17

Baby S. This male child was born at the Women's Hospital, Melbourne, on December 10, 1948, and weighed three lb. 8 oz. (1,600 gm.) at 28 weeks' gestation.

When examined on June 20, 1949, the right disc was covered with connective tissue, giving it a fuzzy appearance, and gave the appearance of a coloboma. In the left fundus there was a retinal fold stretching from the disc to the ora serrata in the temporal retina. One and a half years later the fundus appearance was unchanged and the child had sufficient vision to see small coins.

CASE 18

Baby R. S. This girl was born at the Women's Hospital, Melbourne, on May 8, 1949, at the 26th week of gestation and weighed two lb. 9 oz. (1,160 gm.). Eight weeks after birth it received a transfusion for anemia.

When examined on July 28, 1949, there were complete retrolental membranes, with multiple hemorrhages on the surface, in each eye. No red reflex could be obtained. Three months later the condition was unchanged.

CASE 19

Baby T. This male infant was born at the Women's Hospital, Melbourne, on October 14, 1950, at 30 weeks' gestation and weighed three lb. 8 oz. (1,600 gm.). It was first examined on November 10, 1950, and the blood vessels in the right fundus were found to be somewhat dilated and there was a dense vitreous haze in the left eye.

When examined four weeks later, there were large gray masses in the peripheral retina of the right eye and, in the left eye, there was a gray mass, 10 disc diameters across, situated at the posterior pole of the eye. The vitreous opacities were less.

A month later, the masses in the right eye were smaller and the gray mass in the left eye was whiter and resembled choroiditis. Two months later this mass was still smaller and the vitreous opacities were larger and more discrete, so that a better view could be obtained of the fundus. The child is still under observation.

CASE 20

Baby T. This male child was born at the Women's Hospital, Melbourne, on April 12, 1948, weighing three lb. 3 oz. (1,450 gm.) at 28 weeks' gestation. He was examined on July 17, 1950, when it was found that he was only able to distinguish large objects (such as a pencil held at a distance of one meter).

Examination under a general anesthesia showed that, on the posterior surface of the right lens, there was a thin connective-tissue membrane covering the lower half of the surface. The fundus could be seen by looking over the membrane and it was normal. The posterior surface of the left lens was completely covered by a fine membrane through which, however, a red fundus reflex was obtainable, although no fundus details could be seen.

The child was mentally retarded. At the age of three years, he was not as advanced as his two-year-old sister.

CASE 21

Baby T. This male child was born at the Women's Hospital, Melbourne, August 15, 1950, at 36 weeks' gestation and weighed three lb. 7 oz. (1,570 gm.). When examined on January 12, 1951, there was a complete retrolental membrane in each eye and the anterior chambers were very shallow. A thin fibrous tissue membrane occluded both pupils. When seen on September 14, there was no change in either eye.

CASE 22

Baby W. This male infant was born at the Women's Hospital, Melbourne, on January 27, 1948, weighing two lb. 5 oz. (1,050 gm.), at the 26th week of gestation. It had an infected cord for which penicillin was given and, a fortnight after birth, developed pneumonia. A month later a transfusion was given because the hemoglobin had fallen to 64 percent.

When seen on November 18, 1948, the fundi were pale and there were grayish masses at the periphery. When seen on July 13, 1951, both fundi showed large white areas of degeneration and there were incomplete retrolental membranes.

CASE 23

Baby W. This girl was born at the Women's Hospital, Melbourne, on June 14, 1950 at 29 weeks' gestation and weighed two lb. 14 oz. (1,300 gm.). Two days after birth it was edematous and its hemoglobin was 162 percent. Neptal was given. On July 15, 1950, it developed an upper respiratory tract infection for which streptomycin and penicillin were given. On July 29, 1950, a transfusion was given.

When the eyes were first examined a month later, there were large gray masses in the right fundus and many vitreous opacities. The left eye showed a complete retrolental membrane over which coursed fine vessels.

A month later there were complete membranes in both eyes and the anterior chambers were very shallow. A month later synechias were present in the left eye.

108 Collins Street (C.1).

My thanks are due to Miss Ida Mann for assistance with this paper, and to Dr. Kate Campbell, Dr. A. S. Anderson, Dr. A. Cunningham, Dr. J. Nattrass, Dr. P. E. Jeffery, and Miss S. Plaisted for help in various ways.

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CONGENITAL AND FAMILIAL ENDOTHELIAL DEFECTS*

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The common feature of this case group is seepage of the aqueous, through congenital or acquired defects in Descemet's membrane and its endothelial lining, into the corneal stroma with serious effects upon its clearness and vitality. In the acquired group are those cases of traumatic defects due to birth injury or which may develop, usually in older persons, without known cause. The birth-injury group is easy to diagnose and will not be included in this paper.

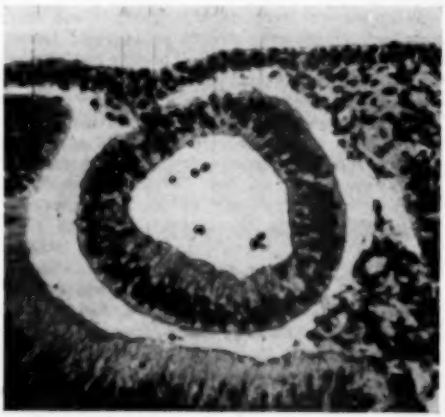

Fig. 1 (Levitt and Lloyd). Embryonic lens separating from the ectoderm. (Reprinted from Fischer: Arch. f. Ophth., 130:517, 1930.)

The etiology of the congenital cases was traced some years ago because other serious defects shortened the lives of the infants involved. At first cloudy corneas of infants were thought to be scars of healed ulcers or, if seen very early, were attributed to intrauterine inflammation. When the defects in the postcorneal surface were first noted, the term internal corneal ulcer was used. Peters, however, showed that these lesions were due to defective separation of the ectoderm (fig. 1) and the lens anlage, associated with other defects following delayed or defective formation of the anterior chamber.

The associated defects include embryotoxon corneae posterius, persistent pupillary membrane remnants (some attached an-

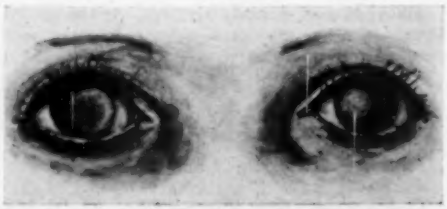

Fig. 2 (Levitt and Lloyd). Baby L. Congenital corneal opacities.

* Presented at the 86th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, June, 1950.

teriorly) pyramidal and anterior polar cataracts, and congenital hydrophthalmus.

As an example of congenital corneal clouding, we have the eyes of Baby L., delivered with forceps, January, 1950, without marks of any kind upon the face or head, and examined within the next 24 hours.

Both corneas showed an oval bluish gray cloud (fig. 2) involving the stroma of the nasal two thirds of each cornea in the ocular fissure. At the nasal side of the left limbus was a small congerie of vessels which disappeared in the first few weeks. The conjunctivas were clean and white, eliminating as cause the effects of silver nitrate or other irritating material. There were no signs of syphilis and the mother's Wassermann reaction was negative.

The child had lateral nystagmus with periodic spastic turning down of the eyes and was not interested in a test light. By the 10th week the nystagmus has lessened and a flashlight attracted her attention.

A few such cases have been reported with microsections and, from the report by Mohr (figs. 3 and 4) the lesions of a similar case are shown, with bleb formation, and later lessening of the involved area. The section shows the large defect in Descemet's membrane and its endothelial covering and the changes in the corneal epithelium and the stroma beneath.

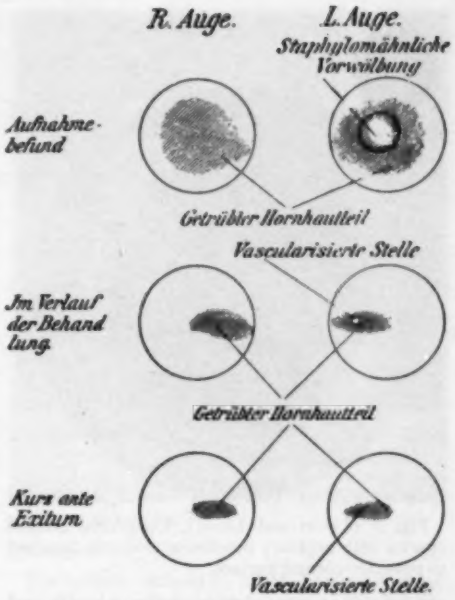

Fig. 3 (Levitt and Lloyd). Congenital corneal opacity. Two months between first and last illustrations. (Reprinted from Mohr: Klin. Monatsbl. f. Augenh., **48**:(2) 340, 1910.)

Another type of congenital defect is the

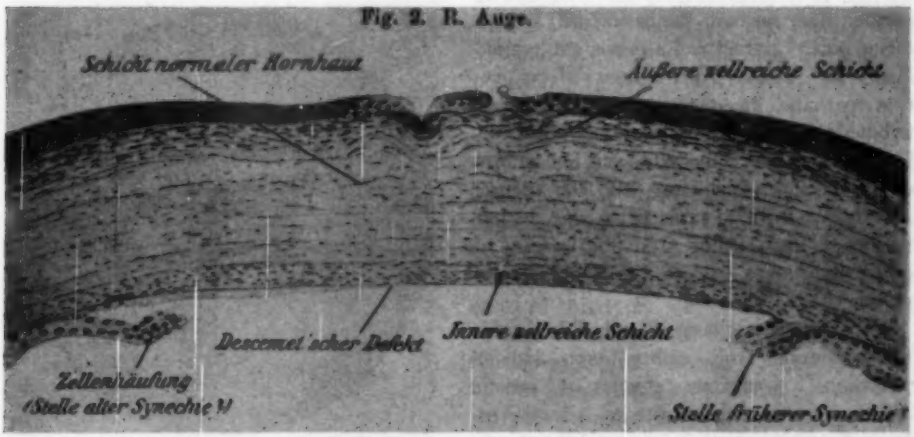

Fig. 4 (Levitt and Lloyd). Congenital defects in Descemet's membrane and endothelium. This is a section of the left eye shown in Figure 3. (Reprinted from Mohr: Klin. Monatsbl. f. Augenh., **48**:(2) 340, 1910.)

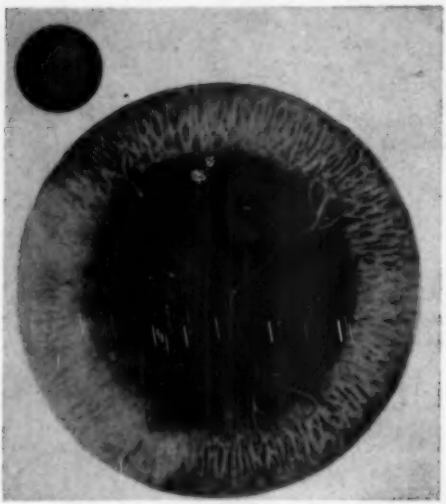

Fig. 5 (Levitt and Lloyd). Congenital corneal opacity with pupillary membrane remnants attached to posterior corneal surface.

superficial opaque sector continuous with and of the same color and appearance as the sclera. It gives the impression that this particular sector retained the opacity of the embryonic cornea (fig. 5).

The stroma is not entirely clear elsewhere particularly in the region where persistent pupillary-membrane strands are attached to the posterior corneal surface. The eye is smaller than normal, the vision nil, an anterior polar cataract and a persistent hyaloid artery are present. All of these defects, except, perhaps, the opaque sector can be attributed to defective separation of the embryonic lens from the ectoderm and subsequent seepage of aqueous into the corneal stroma. We have no explanation why the one sector did not change from the opacity of early embryonic life to the normal clear cornea.

Congenital cases seen in early life require differentiation from embryotoxon and its variations, pernicious effects of caustic agents (overstrong nitrate of silver), inherited syphilis, birth injury, and the cloudy cornea of congenital hydrophthalmus.

Typical embryotoxon is easily distinguished but there may be opaque sectors running into the corneal layers. The opacity of birth injury is a unilateral porcelain-white opacity due to a misplaced forceps tip pressing the eye against the pulley of the superior oblique. Congenital syphilis should not be difficult to diagnose.

Familial incidence

Instances of congenital corneal opacities occurring in families have been reported and we report the eyes of three adults in a family of six siblings. The parents are Italian and second cousins. The children of the T. family are:

Sibling	Age (years)	Status
John	30	Affected
Son	34	Normal
Daughter	35	Not seen
Frances	37	Affected
Benny	42	Affected
Son	44	Normal

Case 1

John, aged 30 years, is married, has normal six-year-old daughter, and works as a roofer. He came to Dr. Place's clinic at the Brooklyn Eye and Ear Hospital in October, 1949. His parents recognized defective vision at birth. He attended sight-conservation classes and finished three years of high school but had to stop because of his eyes. He never wore glasses.

Vision: O.D., 20/300 with a −2.25D. sph. ⊃

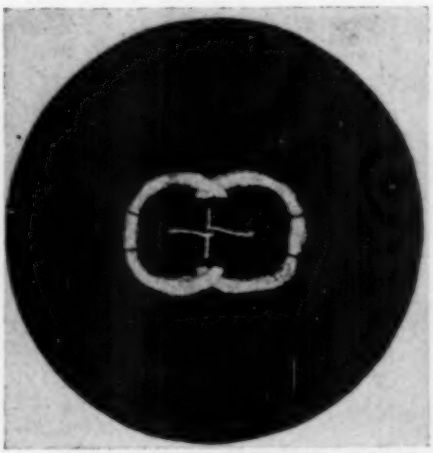

Fig. 6 (Levitt and Lloyd). J. T., right eye, vision: 20/70, with correction. Distorted image of the ophthalmometer mire.

−2.5D. cyl. ax. 30° = 20/70; O.S., 20/300 with a −2.25D. sph. ⊃ −2.5D. cyl. ax. 150° = 20/60.

Glycerin clears the cornea somewhat but not enough to allow a view of pupil or fundus. Tension: normal, O.U. (fig. 6).

CASE 2

Frances, aged 37 years, is single and has been employed as a feeder in a candy factory for 15 years. She has a speech impediment and is hard of hearing. She did not talk until 10 years of age, is very shy, and never attended school. She never wore glasses. Vision: O.D., 20/100 with a −1.0D. sph. ⊃ −1.5D. cyl. ax. 90° = 20/70; O.S., 2/400, not improved. There is slight horizontal nystagmus. The left cornea is very cloudy and waterlogged and stains diffusely with fluorescein. Tension: Normal, O.U.

CASE 3

Benny, aged 42 years, is married and has one normal daughter, aged 15 years. He is employed as a "stayer" (putting corners on paper boxes).

He learned Braille in a school for blind, then attended sight-conservation classes up to 7B in grammar school. He has been treated for his eye condition in various places. In 1948 he attended the Long Island College Hospital where tension was found to vary from 33 to 50 mm. Hg for the right eye and 26 to 38 mm. Hg for the left by McLean tonometer.

Vision at the first visit: Fingers at one foot and light perception, improved to 2/60, O.U.

When seen by Dr. Levitt vision was: 4/400 and 10/400 and was improved by a −9.0D. sph. to 15/400 and 20/200. Glycerin clears the cornea very much for a time. In February, 1950, the tension was 30 and 18 mm. Hg (Schiøtz). Vision is much improved on a clear sunny day and dimmer when cloudy or rainy (fig. 7).

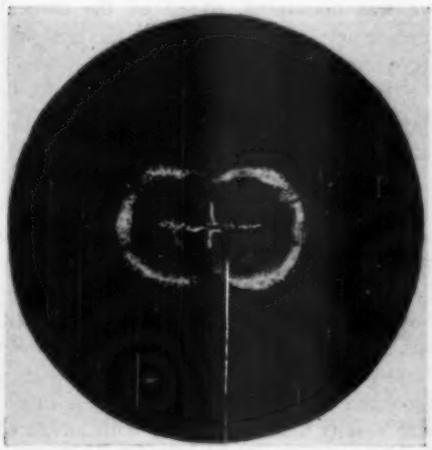

Fig. 7 (Levitt and Lloyd). B. T., left eye, vision: 20/200. Distorted image of ophthalmometer mire.

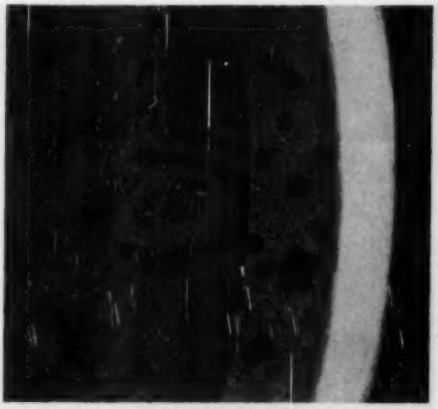

Fig. 8 (Levitt and Lloyd). Mrs. P. Vision: 20/30, varies from day to day. Cornea guttata.

COMMENT

The corneal surfaces of all of these patients are smooth and polished but undulating, as the illustrations of the ophthalmometer mires of the two men show, except when Benny's tension is raised or the left eye of the sister shows edema of the cornea. The cloud is definitely in the corneal stroma, involves the entire cornea, and obscures the pupils.

We hope to be able to continue observation of the eyes of the children of these siblings to see if changes similar to those of the T. family appear.

In 1910, Fuchs described an epithelial dystrophy of the cornea featured by surface edema, lowered sensitivity and vitality, and a marked tendency to glaucoma. Some years passed before Vogt, Basil Graves, and Harry and Jonas Friedenwald, using the slitlamp, associated these lesions of the anterior surface of the cornea (fig. 8) with the antecedent endothelial dystrophy commonly referred to as "cornea guttata." Later Vogt and Verhoeff reported the microscopic features found on the posterior corneal surface in cases of this type.

Goar has pointed out that many older persons have typical "cornea guttata" without serious interference with vision or anterior-surface changes later. Nevertheless, the change from a quiet eye with typical cornea guttata to the serious state of Fuchs's dystrophy does occur spontaneously, after

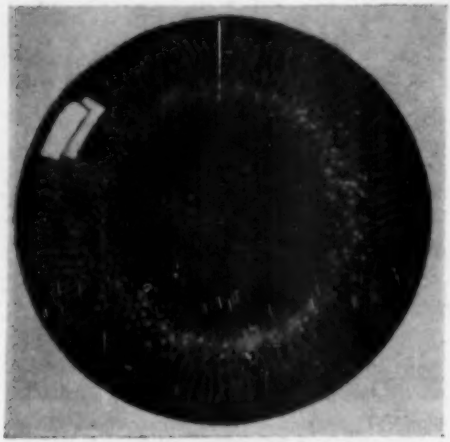

Fig. 9 (Levitt and Lloyd). Early stage of Fuchs's dystrophy.

cataract surgery or debilitating illness and may be familial.

We would refer first to a mother and daughter with the typical endothelial changes to illustrate the vagaries of the Fuchs's type.

Mrs. L. has been under observation for 16 years. The posterior bedewing was first noted six years before lens changes required a combined intracapsular extraction. Not even the slightest aggravation of the condition has been noted in the four years since.

The daughter has been under observation for 28 years, coming first at the age of 13 years for left convergent strabismus, with vision of 20/20 in the right eye and 10/70 without improvement in the left. During the past eight years, the right eye has suffered attacks of surface edema and sharp lowering of acuity. The amblyopic eye, with the same bedewing of the posterior surface of the cornea, has never given trouble and neither mother nor daughter have shown an increase in tension. Complaint was first made at the age of 21 years.

Upon awakening the vision was blurred but cleared later in the day (fig. 9). After several of these attacks, she came to the office with the vision down to 20/40 and a patch of corneal edema over the pupil area. She now wears an "expansion shield" steadily and has had no attacks for the past three years.

An example of activation of bilateral cornea guttata by cataract surgery is the case of Mr. A. B., aged 56 years, who came because vision of the left eye dropped to finger counting at three feet in two years. With the right eye he could read 20/20 less a few letters, the lens was clear except for a sector in the temporal periphery. Operation was not advised at that time but postcorneal bedewing was noted in both eyes.

A year later the cloudy sector of the right lens involved the pupil area and operation upon the left eye was done by Dr. Buonagura with complete success. Soon after the cornea was uncovered, its surface became cloudy, the eye became irritable and sensitive to light, and the sensitivity dropped. Pilocarpine and dionin were used and an expansion shield was fitted to the spectacle frame.

After two months the vision improved from 10/100 to 10/20 with correction and later became 20/25, J1. He carried the shield about with him but has had no occasion to use it recently. In the next year the vision of the right eye failed rapidly and he asked that it be operated. Dr. Buonagura operated successfully but, when the cornea of the right eye was uncovered, edema of the corneal surface developed (as it had in the left eye) and the vision dropped to 10/200.

The vision improved in two months to 20/40, J2, using the protective device and dionin locally. The cornea is insensitive to a wisp of cotton and the typical bedewing of the posterior surfaces is now as it was when he was first seen. In addition, there are bits of fibrin in the eye recently operated.

In neither of these cases operated for cataract have we ever seen contact of vitreous and posterior corneal surface and both cases were studied under the slitlamp as soon after the operation as practical. Less favorable results after operation, with advanced changes of the anterior corneal surface and final loss of vision, are illustrated in Figure 10.

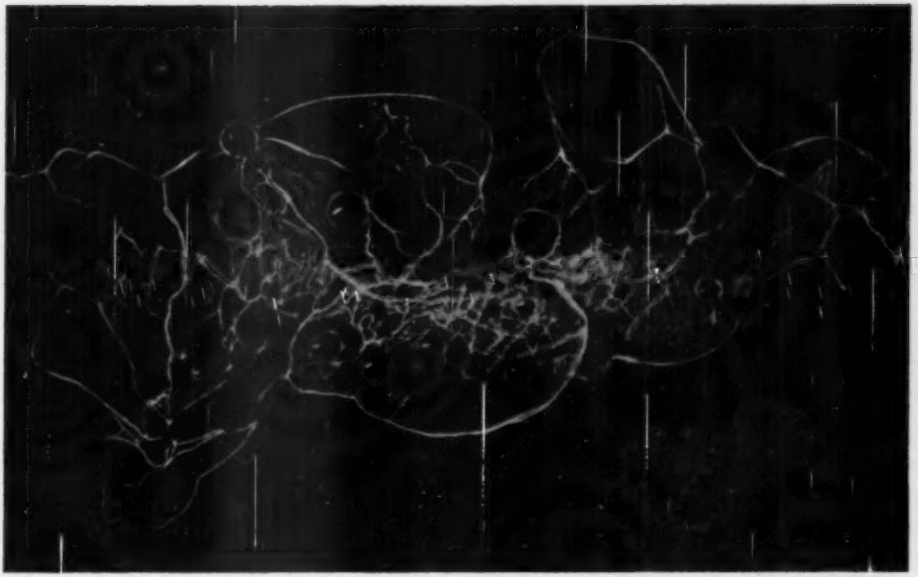

Fig. 10 (Levitt and Lloyd). The patient in this case was aged 74 years. Epithelial dystrophy four months after cataract extraction.

A debilitating illness may also provoke a quiet case into vicious activity. Miss C., aged 67 years, broke an ankle and was confined to bed for a month. She was grossly overweight and there were complications that prevented her from getting about and delayed attention to the eyes which read 6/200 and 12/200, with both corneas cloudy and edematous at the first visit (fig. 11). The protective device was used and the eyes became white and quiet but, owing to the dense layer of the new tissue beneath the epithelium, vision was down to large objects.

Although there were no signs of glaucoma at the time, pilocarpine was prescribed for steady use in each eye at night. After a time she stopped its use and, when seen one year later, both eyes were hard and vision nil. The marked tendency to glaucoma in advanced

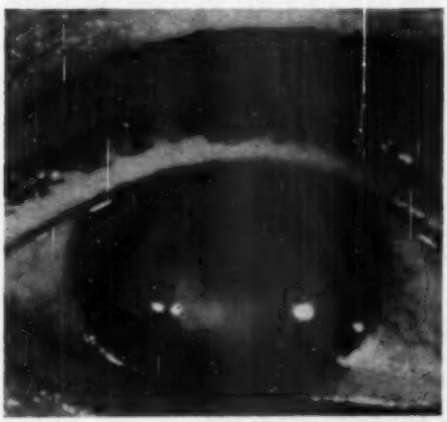

Fig. 11 (Levitt and Lloyd). Miss C., aged 67 years. Late stage of Fuchs's dystrophy. Eye is quiet but vision is very poor because of subepithelial tissue.

Fig. 12 (Levitt and Lloyd). Moist chamber attached to right spectacle lens. Expansion shield attached to left spectacle lens is removable.

endothelial dystrophy suggests that we have not yet found the real cause of the disease (fig. 12). It is impossible to tell in many cases whether the dystrophy preceded the glaucoma or not.

Corneal edema, with lowered sensitivity and tendency to formation of blisters and ulcers, is found in herpes, its recurrences, and sequellae; but is limited to the surface primarily.

Discussion

Dr. F. H. Verhoeff: The endothelium of the cornea looks like a simple tissue which, if injured, would immediately restore itself. On first impression, it is difficult to see how it could cause any lasting trouble. But when we consider the matter further, we realize that the endothelium is a very special tissue, different from any other in the body. The embryologists have pointed out that it is not endothelium like the endothelium of the blood vessels and lymphatics. It should not be called endothelium but it has been called that so long that the error will continue to persist.

What makes the endothelium so peculiar is that it can produce new Descemet's membrane. We might say that Descemet's membrane is like the internal elastica of the arteries but it is not certain that the internal elastica of the arteries is produced by endothelium and Descemet's membrane does not stain like the elastic tissue of the arteries. I do not know of any other simple layer that will produce a tissue like Descemet's membrane. It does not depend for this on the tissue underneath it, because it will produce Descemet's membrane on the iris too.

Cornea guttata can occur rather early in life and exist for years without epithelial dystrophy. I do not know how constantly it leads to epithelial dystrophy, probably it always will finally, but it is evident that the cornea guttata itself does not do so. Presumably the endothelial dystrophy is due to abiotrophy, which means premature senility of the tissue concerned.

Premature senility is often at first associated with hyperplasia; thus, in keratosis of the skin there is hyperplasia of the epithelium. There is quite a similarity between the retinal pigment epithelium and endothelium in that, as a result of the hyperplasia, both may produce wartlike excrescences and both may produce hyalinelike tissue.

Finally, as the last stage of abiotrophy, both tissues may die. In the case I reported, which was published by Dr. Lloyd (Am. J. Ophth., 27:237, 1944) in one of his papers not long ago, the pigment epithelium showed just as marked changes as the corneal endothelium and in places complete necrosis. It seems that what happens in these cases is an endothelial abiotrophy at first associated with hyperplasia and the production of new tissue such as warts and/or new Descemet's membrane and later with death of the endothelium, permitting fluid to get through the cornea and produce the epithelial damage.

14 Eighth Avenue (17).

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CORNEA GUTTATA AND FUCHS'S DYSTROPHY

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SUCCESSFUL CORNEAL GRAFT IN A CASE OF ENDOTHELIAL AND EPITHELIAL DYSTROPHY*

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Experiences with corneal transplants in cases of Fuchs's dystrophy have been discouraging. Owens and others[1] report that in none of the 10 cases of Fuchs's dystrophy reported in this country in which a corneal graft had been done had the graft remained clear four months or longer. They conclude: "Total failure resulted in every instance in cases with Fuchs's dystrophy of the cornea."

Castroviejo[2] lists Fuchs's epithelial dystrophy among the conditions that do not lend themselves to keratoplasty. And Roberts[3] reporting 100 cases of corneal transplantations done at the Manhattan Eye, Ear, and Throat Hospital states that all three cases of Fuchs's dystrophy included in his series were failures and concludes that keratoplasty is contraindicated in this disease.

The European literature does not contain such definite judgements; however, the results are difficult to compare because in the statistics available corneal dystrophies are usually referred to as a group without clearly differentiating the various types (Nizetic[4]).

Paufique, Sourdille, and Offret,[5] in their exhaustive report on corneal grafting presented to the French Ophthalmological Society in 1948, concur in that the chance of success for corneal grafts in Fuchs's dystrophy is very slim, but they seem to have had at least some partial successes. Personally, I had, up to recently, done keratoplasty only in one case of Fuchs's dystrophy, which also was a failure.

I have been studying the pathology, pathogenesis, and the clinical course of endothelial and epithelial corneal dystrophy for several years and shall report on the results in detail in the near future. From these studies, it became apparent that, certain conditions prevailing, corneal grafting might be successful even in the presence of Fuchs's dystrophy, if the cases were properly selected. The case to be reported here gives proof of this possibility.

CASE HISTORY

C. W. H. (No. 109,345), a 60-year-old white man, was first seen at McPherson Hospital as an out-patient on June 6, 1950. Gradual loss of vision in both eyes over a period of several years was reported.

Vision: R.E., without correction, 10/400; with a +1.5D. sph. ⊃ −2.0D. cyl. ax. 100° = 20/100; L.E., without correction, 10/400; with a +1.0D. sph. ⊃ −1.5D. cyl. ax. 95° = 20/200.

* From the McPherson Hospital and Duke University School of Medicine.

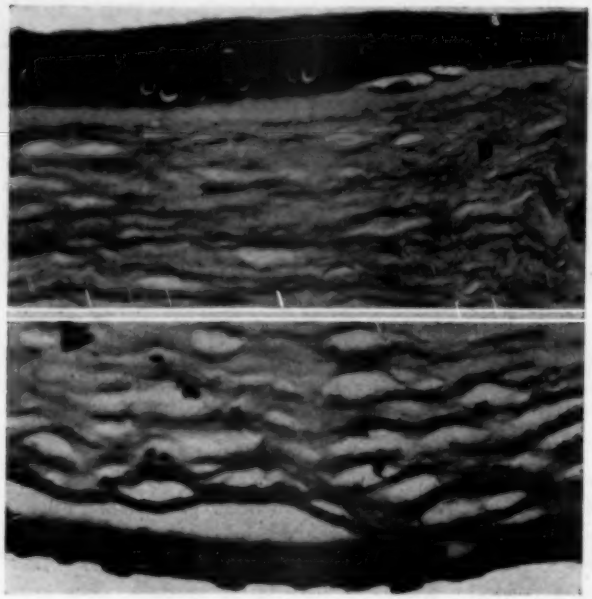

Fig. 1 (Stocker). Section through piece of cornea removed from host. Irregularity of epithelium with signs of edema and beginning bullae formation (apart from artefacts). Corneal lamellae irregularly arranged and with fewer nuclei which are degenerated. Note particularly that Descemet's membrane is considerably thicker than Bowman's membrane and shows excrescences. The endothelium is completely degenerated.

The diagnosis of bilateral Fuchs's endothelial and epithelial dystrophy was made and hospitalization was advised for further study and possible keratoplasty. On admission, October 25, 1950, the following condition was found:

Right eye. Macroscopically, a faint haziness comprising the central part of the cornea could be seen. This area did not exceed five mm. in diameter. With the slitlamp, in this area the epithelium was found to be edematous and some small bullae were present. The stroma was imbibed with fluid and the endothelium reduced to occasional cells. Farther to the periphery, however, the corneal edema was absent and a fair amount of healthy endothelium could be seen. No vascularization of the cornea was present.

The anterior chamber and iris were not remarkable. The lens showed moderate nuclear sclerosis. The fundus could not be seen in detail.

Vision: 20/200, with correction.

Left eye. Almost exactly the same condition existed as in the right eye. Vision: 20/100, with correction.

General physical examination revealed essentially normal conditions.

The diagnosis of endothelial and epithelial dystrophy was confirmed. The patient was given full information as to the generally poor prognosis of keratoplasty in cases of this disease. However, it was explained to him that it was felt that his particular case might present a better than average chance due to the confinement of the lesion to the central parts and to the presence of a fair amount of healthy endothelium in the peripheral parts of the cornea. Considering the fact that his vision had become progressively worse and most certainly would continue to do so, the patient was willing to take a chance with the right eye which appeared to be the worse.

On October 26, 1950, a partial perforating circular corneal transplant, 7.5 mm. in diameter, was done, using for donor material an eye obtained through the courtesy of The Eye-Bank for Sight Restoration in New York. The graft was sutured into place with nine edge-to-edge sutures, using the special Grieshaber needles. A perfect adaptation was obtained.

The piece of cornea removed from the patient's eye was examined pathologically. Changes typical for endothelial and epithelial corneal dystrophy were found (fig. 1).

Beginning on the 15th postoperative day, one drop of 1.25-percent suspension of cor-

Fig. 2 (Stocker). (Right) Large circular corneal graft, apparently clear. Vision: 20/20, with correction. (Left) Haziness in central part of cornea due to endothelial and epithelial dystrophy. Vision: 20/200, with correction.

tone acetate was instilled into both eyes every two hours. During this treatment, the graft, which never had shown but only slight haziness, became clearer and clearer. Also the cornea in the nonoperated eye improved to some degree. The bullae formation of the epithelium and the water content of the stroma diminished and the transparency increased. After one month, cortisone was reduced to every four hours, and after two months to four times a day. On February 7, 1951, the graft was found to be perfectly clear. The endothelium on the graft was clearly visible. There were a few Henle's warts. Vision, with a +5.0D. sph. ⊂ −6.0D. cyl. ax. 155° = 20/20. Glasses were prescribed.

On May 9, 1951, the condition of the right eye was unchanged. Vision was 20/20, with correction (fig. 2). On December 5, 1951, the condition was unchanged.

Comment

Why was keratoplasty in this case of Fuchs's dystrophy successful and why was the operation a failure in most of the reported instances?

Apparently an intact endothelial layer is indispensable to keep the graft from becoming diseased. We have seen a graft acquire a condition very closely simulating Fuchs's dystrophy after observing that Descemet's membrane had detached itself from the stroma during the postoperative course, without the recipient cornea suffering from this disease.

Consequently, if the graft is placed in an environment that contains practically no endothelium, it is likely to degenerate with endothelial and epithelial dystrophy. On the other hand, it often can be seen that Fuchs's dystrophy begins in the central parts of the cornea with most of the endothelium gone in that area; whereas, toward the periphery, large patches of normal endothelium are still present.

If a graft with normal endothelium, sufficiently large to replace most of the diseased central part, is transplanted, there might be a possibility of the graft's endothelium joining up with the comparatively healthy endothelium of the recipient. The latter condition was present in the case herein reported.

Also of importance to success is the use of the sharp Grieshaber needles for direct suturing; these help to give better coaptation of a rather large (7.5 mm.) graft.

The donor material should be obtained from a comparatively young person, minimizing the possibility of transplanting a graft that might already have acquired a senile degeneration of the endothelium.

Summary

A case with typical Fuchs's endothelial and epithelial dystrophy is reported in which a keratoplasty has been successful, the graft being clear after more than one year and

vision improved from 20/200 to 20/20.

The reasons for success and failure of keratoplasty in cases of Fuchs's dystrophy are discussed. It is thought that the possibility of success is dependent on the following factors:

1. Cases with complete degeneration of the entire cornea should be excluded and the operation reserved for cases that show considerable disease in the central part of the cornea, with vision markedly reduced, but a fair amount of endothelial cells still present in the peripheral parts.

2. The graft should be rather large; if possible all of the definitely diseased parts of the cornea should be replaced.

3. The graft should be held in place with 8 to 12 direct sutures, using special Grieshaber needles.

4. Donor material should be derived from a young person (less than 40 years of age).

5. The topical use of cortisone during the postoperative course seems to have a beneficial effect, not only on the graft, but also on the dystrophy itself.

1110 West Main Street.

At time of proofreading, another case of Fuchs's dystrophy had been successfully grafted, using a subtotal perforating graft, nine mm. in diameter, with graft being perfectly clear and vision 20/20, corrected, after more than two months.

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AN EXPERIMENTAL STUDY OF THE POSSIBILITY OF TRANSMITTING SYPHILIS BY A CORNEAL GRAFT*

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The purpose of this experiment is to determine whether or not syphilis can be transmitted fom one animal to another by means of a corneal graft. From the point of view of the clinician performing a corneal graft operation, the pertinent question is: "Can syphilis be transferred from donor to host if the donor's eye is free from all evidence of past or present inflammation even though the donor has an undetected early or latent syphilis?" This question was investigated experimentally.

* From the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University. Candidate's thesis for membership in the American Ophthalmological Society accepted by Committee on Theses.

Literature

It has been abundantly demonstrated that syphilis can be transmitted by blood transfusion during certain early stages of the disease. Uhlenhuth and Mulzer,[1] and Frühwald[2] showed that the blood from patients in the primary stage of syphilis transmitted the disease in 84.2 percent of cases tested. In secondary syphilis, they found the transmission incidence to be 75 percent.

Brown and Pearce[3] have shown that the blood of a syphilitic rabbit becomes so infectious between the seventh and 14th day following inoculation that 5.0 cc. will transmit the disease. They concluded that the syphilitic virus is present in the blood during the acute

or active stage of the infection and, with the disappearance of active lesions, the blood loses its infectiousness.

Eberson and Engman[4] tested blood from 73 individuals with latent or chronic syphilis by injection into rabbits' testes. The results were negative.

The blood of patients in the incubative (sero-negative phase) of syphilis is apparently infectious. Morgan[5] reported 16 cases; Salkind,[6] 39 cases; Klauder and Butterworth,[7] 35 cases; and Eichenlaub and Stolar,[8] 41 cases. In these patients with early incubative syphilis they found the blood of such individuals was infectious.

On the other hand, according to Morgan, there is not a single instance reported of indubitable transmission of syphilis by transfusion in which the disease was transmitted by blood from a donor with well-established latent or chronic syphilis (uninfluenced by pregnancy).

McNamara,[9] in an emergency, was forced to transfuse nonsyphilitic patients with blood from chronic syphilitics. No evidence of infection was found from four to five months after transfusion. McCluskie[10] states that, in his experience, infection during the tertiary stage does not occur even though the Wassermann reaction of the blood is positive.

Despite these rather conclusive statements, Moore[11] emphasizes that it is not possible to set any definite time limit on the infectiousness of blood, since cases have been reported where symptoms have occurred from donors infected at least seven years. He states that, in blood transfusion, the best practical method of avoiding syphilitic infection is the rejection of all possible donors with syphilis.

Stokes[12] also vigorously emphasized that the clinical principle of avoiding transfusion infection is not to use blood or serum, spinal fluid or tissues of persons known to have had syphilis without adequate sterilization.

Turner and Diseker's[13] report indicates that the risk of transfusion syphilis is minimized by the use of blood banks. They showed that, in isolated rabbit blood or tissue extract, treponemas apparently do not survive longer than 72 hours. They conclude that under conditions obtaining in blood banks, the treponema undergoes complete deterioration in citrated whole blood during the usual storage period. There is a risk in the transmission of syphilis by transfusion with freshly stored blood but blood stored for four days or longer will no longer transmit the disease.

It is interesting to note that their experiments were performed with fresh tissue extract which contained obviously motile treponemas from which transfusion syphilis would be expected to occur.

While it thus appears well established that in latent syphilis, the possibility of transmission by blood transfusion is minimal, this apparently is not true with tissue extracts. Eberson and Engman[4] isolated treponemas in five instances from latent syphilitics—three times from inguinal glands and twice from the semen. The tissue extracts produced typical syphilitic lesions when injected into a rabbit's testis from which it could be recovered and propagated indefinitely.

This investigation seems to demonstrate that those persons giving a history of an old syphilitic infection may harbor active treponemas in the tissue for years although the Wassermann reaction may be negative or only slightly positive with cholesterinized antigens.

There is considerable evidence that treponemas are present in the eyes of congenital syphilitics in the first stages of the disease even though the eyes are free of clinical inflammation. Yoshida,[14] Rumbaur,[15] and Friedenwald[16] made histologic examinations of the eyes of syphilitic fetuses and stillborn syphilitic infants and found minor changes throughout the uveal tracts in a large percentage of such eyes. Treponemas in the noninflamed corneas of such eyes have been

demonstrated by Stock,[17] Bab,[18] Waetzold,[19] Schlimpert,[20] and von Hippel.[21]

It is, however, not fully agreed that living treponemas are present in the corneas of patients with active interstitial keratitis. In favor of this assumption are the reports of von Hippel[21] who, in 1908, demonstrated by Levaditi's stain that treponemas were present in the cornea of a stillborn syphilitic fetus; of Igersheimer[22] who removed a section of the cornea of a 14-year-old child with active interstitial keratitis and demonstrated treponemas in the stained section; and of Clausen[23] who also found treponemas in the cornea of a four-and-a-half-month-old infant (the child later died of a generalized syphilitic infection).

However, the Leavaditi technique may be misleading and modern syphilologists feel that other proof is necessary to establish the actual presence of the treponema. Further in favor of treponemas being in the cornea is the fact that it has been clearly shown by transmission experiments that they are invariably present in the corneas of experimental syphilitic rabbits with spontaneous interstititial keratitis.

There is, however, some clinical evidence which has been interpreted as indicating treponemas are not present in the corneas of patients with interstitial keratitis. If such corneas did contain treponemas, one might reasonably expect them to be more responsive to antisyphilitic therapy than they usually are. As Duke-Elder[24] states, one would not expect the well-known refractoriness to treatment if the disease was due to the actual presence of the treponemas.

Although it may undoubtedly be difficult for arsenical preparations to reach an avascular structure, such as the cornea, nevertheless, that arsphenamine does reach the cornea is shown by the experiments of Woods and de Schweinitz[25] who demonstrated the immediate beneficial effect from a single injection of arsphenamine in the interstitial keratitis due to trypanosoma infection. The Trypanosoma equiperdum is, however, infinitely more sensitive to arsenicals than are treponemas.

Interstitial keratitis develops only rarely in acquired syphilis. The Coöperative Clinical Group reported only 0.3-percent incidence of interstitial keratitis in 3,244 patients with early acquired syphilis. It is well known that interstitial keratitis occurs rarely in early congenital syphilis where treponemas are widely disseminated throughout the body, but does occur in late congenital syphilis when patients may be receiving strenuous antisyphilitic treatment and when the other syphilitic lesions are progressing favorably. It seems, therefore, that proof as to the actual presence of treponemas in the corneas of patients with interstitial keratitis is not conclusive.

Summing this up, it is quite clear that the blood and tissue extracts of individuals or experimental animals in the early stages of acquired or experimental syphilis are definitely infectious. It has been shown that treponemas are present in the eyes of congenital syphilitics in the early stages of the disease. Woods and Chesney[26] believe they lie dormant in the cornea for years, later producing symptoms of fluctuations of immunity.

The existing evidence, however, indicates that the blood of individuals with latent syphilis is, at best, only occasionally infectious, especially blood isolated from the body for three or four days. It is not established, however, that the tissues are equally noninfectious.

As concerns corneal transplantation, the essential question is—can syphilis be produced in the recipient by the transplantation of a cornea from a syphilitic donor, when the cornea shows no evidence of any old or active inflammation? This question is an immensely practical one, especially in this day of corneal banks and the increasing number of corneal transplant operations.

This question was investigated experimentally in the following manner:

Experiment I

Using 10 rabbits, each with latent syphilis but without a keratitis, corneal grafts were performed, the clear corneas from these rabbits serving as donors.* In none of the donor rabbits was there any clinical evidence of ocular syphilis and, during the course of the systemic syphilis, ocular syphilis had not been observed. In six rabbits, the graft remained transparent; and in four rabbits, the graft became either nebulous or completely opaque. In no host rabbit was there the slightest clinical evidence of syphilitic keratitis.

After three months, the host rabbits were killed. Under rigid aseptic technique, the following procedure was carried out on each rabbit:

The whole cornea containing the graft was removed in its entirety, washed with saline, sliced in several sections, and placed in a mortar to which was added 1.0 cc. of sand and 2.0 cc. of 80-percent normal saline. The corneal tissue was then thoroughly macerated and either centrifuged or allowed to stand for 10 minutes; 1.0 cc. of the supernatant emulsion was then drawn into a tuberculin syringe and 0.25 to 0.5 cc. was injected subconjunctivally into the right eye and the remainder into one testis of a normal male rabbit. These rabbits were observed at periodic intervals and, during a period of eight months, no rabbit developed keratitis or orchitis.

There are two possible reasons for failure of this experiment: (1) Either the cornea of the rabbit with latent syphilis does not contain treponemas or (2) the cornea from which the graft was taken contained treponemas in such small quantities that transmission of the infection was not possible. Perhaps the latter reason is more significant inasmuch as the average graft taken is not more than one seventh to one third of the entire corneal surface.

* These rabbits were obtained from the laboratory of Dr. Alan M. Chesney.

Experiment II

Assuming that the clear corneas of syphilitic rabbits contain treponemas and that the reason for failure in Experiment I was the small number of treponemas in an average graft, it should be possible to transfer syphilis by direct testicular or subconjunctival inoculation of a large amount of corneal emulsion. The following experiment was carried out to explore this point:

Ten rabbits with latent syphilis were used. In none had there been evidence of ocular syphilis in any form. In five rabbits, one entire cornea from each rabbit was used; and in the other five rabbits, both corneas from each rabbit were used.

Using the same aseptic technique as in Experiment I, an emulsion was made of each cornea or corneas and injected subconjunctivally and intratesticularly into normal male rabbits.

These rabbits were observed over a period of nine months and in none was there any evidence whatsoever of keratitis or orchitis. It can be assumed from this experiment that treponemas are not present in the corneas of rabbits with latent syphilis.

Experiment III

To determine whether or not it was possible to transmit systemic syphilis by transferring the corneas from rabbits with active syphilis, the following experiment was carried out:

Twenty rabbits were used. Ten rabbits (Group I) had been inoculated with syphilis from the syphilitic liver of either an ape or monkey and, at the time of the experiment, had syphilitic orchitis confirmed by positive dark-field examination.

The other group of 10 rabbits (Group II) was injected with the Nichols strain of T. pallida. This group developed orchitis within 10 days to three weeks. At the height of the orchitis, both entire corneas from each rabbit in the two groups were excised, emulsified, and injected subconjunctivally and intra-

testicularly in 20 normal rabbits. As in Experiments I and II, the same aseptic technique was carried out.

These rabbits were observed at periodic intervals and, during a period of eight months, there was no evidence of either orchitis or ocular involvement.

This experiment shows that the asymptomatic, noninflamed cornea of a rabbit with active syphilis is noninfectious.

Comment

The Nichols strain of T. pallida is an extremely potent one and has been passed through rabbits hundreds of times and is presumably well adapted to its host. Using this strain, Magnuson, Eagle, and Fleischman[27] have shown that two organisms inoculated intracutaneously produced a dark-field positive lesion in 47 percent of the cases. This was increased to 71 percent with 20 organisms and 88 percent with 200 organisms and, finally, 100 percent with 200,000 organisms. With intratesticular inoculation, one to two treponemas were shown to be regularly infectious.

It seems reasonable, therefore, in view of the negative response in the host rabbits outlined in the experiments herein reported, that the nondiseased, apparently normal corneas of rabbits with latent or active syphilis are noninfectious and do not transmit syphilis when transferred to normal rabbits.

One might assume the following clinical application to this experiment. If the eye from an individual with undiscovered or latent syphilis is used as a donor for corneal grafting, these experiments would indicate that it is highly unlikely syphilis would be transmitted.

Summary

1. The corneas from 10 rabbits with latent syphilis were transplanted to the corneas of 10 nonsyphilitic rabbits without any evidence of the development of keratitis during the period of three months.

2. These 10 corneas were removed in their entirety, emulsified and injected into the subconjunctival tissue of one eye and to one testis of 10 normal rabbits. Over a period of eight months, there was no evidence of keratitis or orchitis.

3. The corneas of 10 rabbits with latent syphilis (one cornea in five rabbits and both corneas in five rabbits) were emulsified and injected into the subconjunctival tissue of one eye and to one testis of 10 normal rabbits. During a period of nine months, there was no sign of either keratitis or orchitis.

4. Both corneas of 20 rabbits with active clinical syphilis were emulsified and injected into the subconjunctival tissue of one eye and to one testis of 20 normal rabbits with completely negative results for syphilis over a period of eight months.

11 East Chase Street (2).

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CORNEAL TRANSPLANTATION USING A CORNEAL CAP*

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INTRODUCTION

The use of a corneal cap in corneal transplantation is not a new idea. Shershevskaya wrote in the monograph, *Transplantation of the cornea using freshly conserved and fixated material,* that "Adamiuk and Petrynya recommended fixing the transplant by small celluloid caps corresponding to the convexity of the cornea and resting firmly in place. Rosengren and Gusnain used contact glasses for fixation of the transplant. Bauer proposed that the transplant be fixed by a silver spatula with apertures at both ends. Fixation of the transplant by spatula and caps has not become very popular."

Pittar[1] has reported a platinum-gold splint which has been used in human cases with satisfactory results. Dryden[2] has experimented with a similar splint which has given good results in rabbits. Fritz[3] also reports success with contact lenses in keratoplasty.

In 1948, at the suggestion of Dr. Herbert M. Katzin,† the present study was undertaken in an effort to improve operative results in corneal transplantation. The purpose of the cap was: (1) To bring the curvature of the transplanted cornea as close to that of the original as possible; (2) to prevent postoperative bulging of the edge of the graft; (3) to attempt to reduce postoperative myopia; (4) to foster firm wound closure

* This work was done under the auspices of the Eye-Bank for Sight Restoration, Inc.

† Director of Research for the Eye-Bank for Sight Restoration, Inc.

Fig. 1 (Worcester). Low-power examination of the anterior segment of a rabbit's eye after the application of a total plastic cap covering the entire cornea for seven days. (a) Loss of corneal epithelium, increased thickness infiltration of the corneal stroma with macula formation. The endothelium is not visualized at this power, but is edematous. (b) The anterior chamber is filled with inflammatory cells and albuminous exudate. (c) The iris is swollen and infiltrated with inflammatory cells. (d) The posterior chamber has inflammatory cells and exudate similar to that in the anterior chamber.

in order to prevent such complications as loss of anterior chamber, anterior synechia, and delayed reformation of the anterior chamber and (5) to learn if the patient could be permitted more freedom of motion postoperatively.

The present study was undertaken to determine: (1) The effect upon the cornea of being completely or partially covered by a cap; (2) the maximum time a cap may be kept on the cornea before reversible changes occur; (3) the effect of a cap upon the healing of the cornea; (4) the design of a cap for this use; (5) which plastic, that could be used with ease for this purpose, would be tolerated by the human cornea; (6) the results of its use in human cases.

Experiment I

Healthy rabbits with normal corneas, as examined grossly and under the slitlamp, were used. Plastic caps which covered the cornea from limbus to limbus were sutured in place and, after varying lengths of time, the eyes were enucleated and sectioned.

Rabbit 1

The eye was removed for sectioning on the first day after the contact lens was sutured over the cornea. Gross examination showed that the epithelium was denuded from the cornea. Slitlamp examination revealed thickening of the cornea and a cloudy stroma. The anterior chamber was not visualized.

On microscopic examination, the epithelium was denuded, the stroma vacuolated, the endothelium was edematous, and the aqueous albuminous.

Rabbit 2

On the third day after the contact lens was sutured over the cornea, the eye was removed for sectioning. Gross examination gave the same findings as for Rabbit 1 except that the cornea was opaque. The microscopic examination was the same as for Rabbit 1.

Rabbit 3

Gross examination the first day after suturing the contact lens over the cornea showed increased corneal thickness and the slitlamp showed the cornea to be hazy.

On the third day, observation was impossible because the clouding of the cornea was so dense. On the fifth day the eye was removed for sectioning. By gross examina-

tion the cornea was opaque. The microscopic examination showed the same findings as for Rabbit 1 and, in addition, the presence of interstitial keratitis and iritis.

Rabbit 4

Seven days after the contact lens was sutured over the cornea, the eye was removed for sectioning. Gross examination showed an opaque cornea. Except for macula of the cornea, the microscopic findings were the same as for Rabbit 3.

Conclusion

Experiment I shows that the rabbit eye does not tolerate being completely covered by a plastic cup and that serious complications ensue (fig. 1).

Experiment II

In this experiment, a partial cap was used instead of a full cap—otherwise, the procedure was the same as in Experiment I. Since it was felt that, under clinical operative conditions, a cap would not have to be kept in place longer than 10 days, no cap was left longer than this period.

Rabbit 5

A six-mm. circular solid cap was sutured in direct contact to the cornea by four 6-0 black-silk sutures. This cap was specifically molded for and applied snugly to this cornea. The course was as follows:

Days After Cap Applied	*Findings*
1	Cornea clear from limbus to cap; appears clear beneath cap
2	Cornea not changed
3	Slight haze of cornea at 2-o'clock
4	No change
5	No change except for slight fullness of limbal vessels at 12-o'clock
6	No change
8	No change
9	Few vessels growing toward superior temporal suture; cap removed; epithelium absent in area where cap had been applied; remaining cornea clear
10	Corneal abrasion healing
11	Corneal abrasion healed
19	Cornea normal except for suture scars

Conclusions

1. Limbal injection did not begin until the sixth postoperative day, corneal vessels not until the 10th day.

2. Vessels entered the cornea and grew toward the sutures but did not progress toward the cap.

3. In the area which had been beneath the cap, the corneal epithelium was absent upon removal of the cap.

4. Any corneal changes present at the end of 10 days were reversible.

Experiment III

Normal corneas which had wounds varying in depth from a superficial trephine scratch to a complete graft were covered with a partial cap. This cap, although it did not cover the cornea from limbus to limbus, did cover the entire area of the trephine wound.

Rabbit 6

A circular cap, like the one used in Experiment II, was applied to the normal cornea following a partial trephination of the cornea.

Days After Cap Applied	*Findings*
2	Cornea clear except for slight infiltration at limbus
3	Infiltration definitely progressing from limbus toward center of cornea
4	Slight increase of infiltration; otherwise no change
6	No change
9	Limbal vessels full; cap removed; epithelium absent in area where cap had been; wound unhealed
14	Infiltration decreasing; wound healing; corneal vascularization present
17	Cornea clearing; trephination wound healed
31	Cornea clear except for trephination scar and vascularization

Conclusion

In all cases tissue repair was impaired and healing of superficial wounds was delayed.

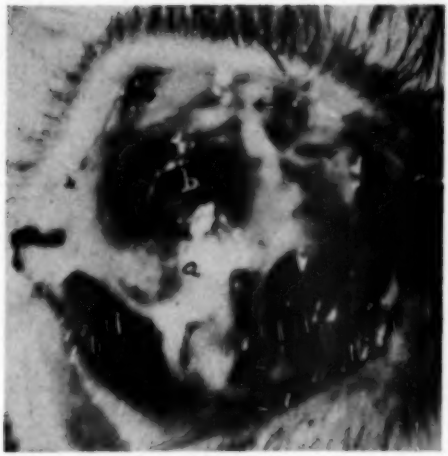

Fig. 2 (Worcester). (a) Plastic cap with four radiating arms and a central perforation (b) sutured over a perforating graft in a rabbit eye.

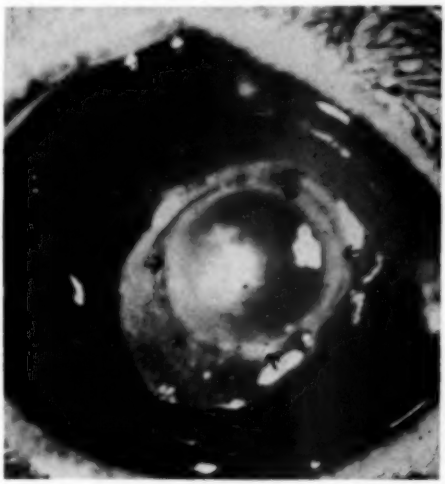

Fig. 3 (Worcester). A successful perforating corneal transplant. The pupil is irregular but within it can be seen the circular scar. The graft is perfectly clear.

Practically no union occurred in the perforating trephination wounds.

Experiment IV

It was evident that to produce the results desired, a cap must fulfill the following requirements:

1. Permit adequate respiration of both recipient and donor corneas.

2. Permit adequate support about the circumference of the wound to obtain a solid union and yet permit maximum exposure of the wound for atmospheric respiration.

Various caps were, therefore, designed and tried. These varied from discs, with various-sized perforations to permit respiration, to triangles with perforations. It was soon evident that another factor must be considered—namely, the circulation of fluid from the limbus to the center of the cornea. Any type of cap with a complete ring about its periphery was soon discarded and replaced by an open type.

The final design—later modified for human cases—was somewhat triangular in that it had three radiating arms, with a large central opening (figs. 2 and 3).

Experiment V

Having produced satisfactory results in the rabbit, a material which the human cornea would tolerate was sought. Since acrylic had been used in the animal work, a six-mm. disc was molded to a normal cornea of a human eye which was to be enucleated. This disc was sutured in the center of the cornea and left for seven days.

At the end of this period, there was slight corneal clouding perceptible under the slit-

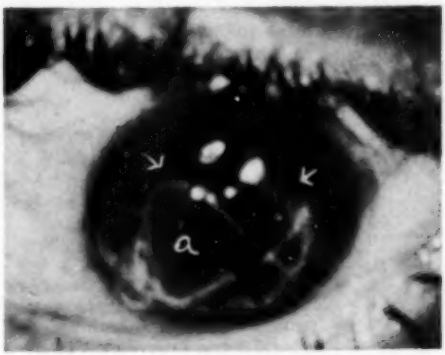

Fig. 4 (Worcester). A solid six-mm. acrylic disc (a) applied to a human cornea by two sutures.

lamp, absence of the epithelium, and slight swelling of the cornea. These changes all cleared within a week.

As this cap was solid and contained a greater surface contact of acrylic than any cap made to hold a graft, it was decided that this material was acceptable (figs. 4 and 5).

Experiment VI

The cap was used in three human cases to hold the grafts in position; all grafts were of the perforating circular type.

Case 1

M. C. was first seen on April 27, 1949, with a history of corneal opacities since the age of 11 years. Examination revealed opacities of both corneas involving all layers.

Vision was: R.E., hand movements; L.E., 20/200. The density of the opacities prevented further observations (fig. 6).

On July 8, 1949, a circular, penetrating, full-thickness corneal transplantation was performed on the right eye, and the plastic cap was used to hold the graft in place. A summary of the postoperative course shows:

Days Postoperative	*Findings*
2	Very little reaction; anterior chamber reformed; slight bulging of the graft at 6-o'clock position

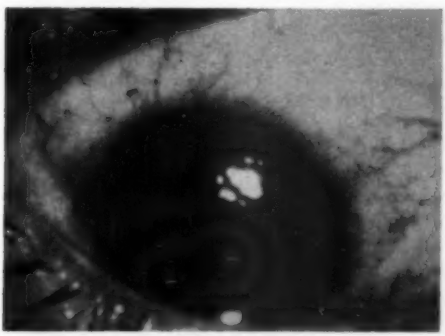

Fig. 5 (Worcester). Same as Figure 4 after the cap was removed. Only suture tracts are visible in the photograph. There is also slight clouding of the cornea.

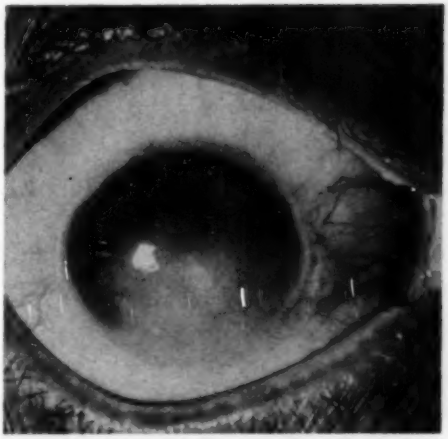

Fig. 6 (Worcester). Preoperative photograph of Case 1 (M. C.).

Days Postoperative	*Findings*
3	No change
5	Suture at 4-o'clock position pulling out
6	Suture at 4-o'clock position pulled out; cap removed; graft bulging slightly from 3- to 6-o'clock; graft slightly hazy, vessels of recipient cornea injected
7	No change
11	Vessels of recipient cornea encircling graft
13	Eye becoming paler
17	Beta irradiation started
18	Discharged from hospital
36	Graft clear; vision, —20/100, unimproved; at this time a membrane behind the graft was found to be the original Descemet's membrane which unknowingly had not been removed at operation*

Later a corneal transplantation was performed on the left eye of M. C., following the technique used for the right eye. A summary of the postoperative course shows:

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*At the time of operation the presence of the original Descemet's membrane was overlooked in the right eye (fig. 7). At the time of operation on the left eye, the cornea split at Descemet's membrane also. Forewarned by the previous experience, the membrane was discovered and removed.

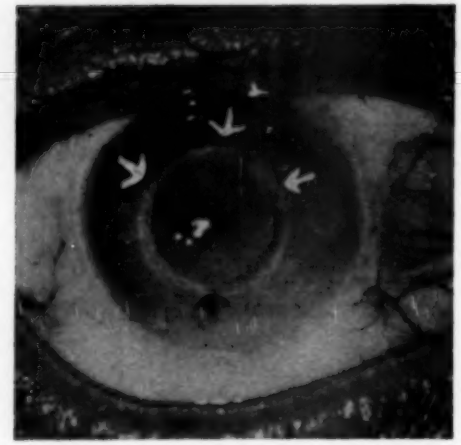

Fig. 7 (Worcester). Postoperative photograph, right eye, of Case 1 (M. C.). Lower half of graft reflex gray due to Descemet's membrane which remained from the original cornea.

Days Postoperative	*Findings*
2	Minimal reaction; cap in place; unable to determine if anterior chamber is definitely formed
3	Minimal reaction; anterior chamber definitely formed; graft is clear
8	Cap removed; graft clear; slight bulging
10	Bulging seen by slitlamp is only graft swollen by edema; posterior surfaces of cornea and graft well aligned
14	Discharged from hospital
16	Graft clear; vision (L.E.) 20/90

Final results

Four months after operation, the grafts in both eyes were clear. Vision was: R.E., 20/200, unimproved; L.E., 20/70, with a -6.0D. sph. $\bigcirc$ -3.25D. cyl. ax. 165°; reads J2.

Comment

There was practically no photophobia following the operation. The cap was well tolerated by both eyes, without pain. There was no bulging of the graft, except in the right eye when one of the sutures began to pull loose on the fifth postoperative day. There was practically no edema of the donor graft, a usual occurrence on the fifth postoperative day when sutures are used.

Postoperatively there were found small, irregularly bound-down pupils and the fundi were never seen in either eye. In the right eye, the original Descemet's membrane remained, and became somewhat more dense, reducing the vision. The grafts in both eyes remained clear and there was no explanation for failure to obtain better vision. Keratometer readings were not obtainable; one might surmise that emetropia existed in the right eye; however, this is open to discussion.

Case 2

M. T. was first seen on November 24, 1948, with a history of myopia, old uveitis, and of poor vision for two years. In July, 1948, a scarification and application of hydrochloric acid to the cornea were done in an attempt to thin the opacity. The opacities involved all layers of both corneas. The vision was 20/200 (fig. 8).

A circular, full-thickness corneal transplantation was performed on the left eye and a plastic cap was applied. The postoperative course showed:

Days Postoperative	*Findings*
3	Good anterior chamber; cap in place
6	Slight reaction; good anterior chamber
8	Cap removed; anterior chamber lost as 12-o'clock suture removed*
9	Anterior chamber reformed; no bulging
13	Discharged from hospital; only evidence of bulging is by slitlamp; vision counting fingers at three feet, uncorrected
22	Graft clear; extreme photophobia and lacrimation; patient readmitted for iridocyclitis; vision, counting fingers at five feet
28	Iridocyclitis improved; graft slightly cloudy
36	Discharged from hospital; graft still swollen and cloudy; vision, counting fingers at five feet
43	Graft clearing; vision improving

* At the time of the operation the surgeon thought this suture passed into the anterior chamber but was not sure.

Fig. 8 (Worcester). Preoperative photograph of Case 2 (M. T.).

FINAL RESULTS

Three months postoperative, the graft was clear. By the fifth postoperative month, the graft was well healed and vision was counting fingers at one and a half feet (fig. 9).

COMMENT

The cap was well tolerated and the graft remained in excellent apposition with the recipient cornea. There was no cause found for the iridocyclitis. Since this occurred three weeks postoperatively and a week after the patient had been discharged from the hospital, the possibility of the cap causing the reaction may be disregarded. Again as in the first case, there is no true evaluation of the postoperative vision. Furthermore, it should be pointed out that neither of these cases had a good preoperative prognosis for vision.

The results in these two cases would seem to show that the cap is tolerated and that better results may be expected on more favorable eyes.

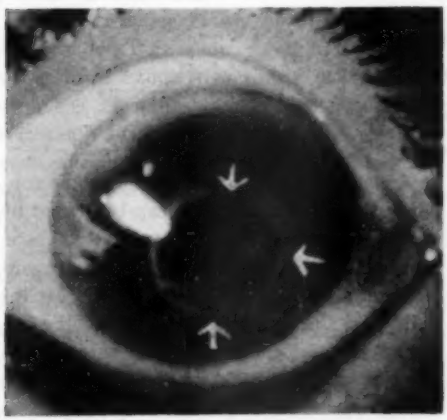

Fig. 9 (Worcester). Postoperative photograph of Case 2 (M. T.).

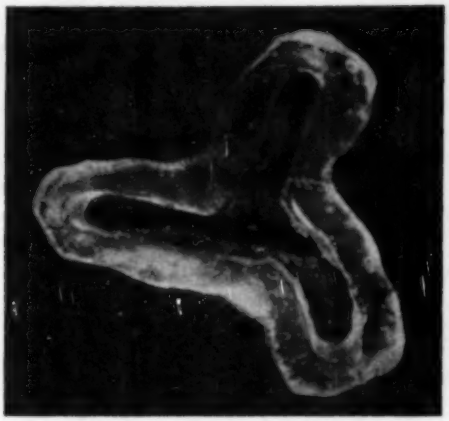

Fig. 10. (Worcester). Plastic cap used in human cases.

Fig. 11 (Worcester). Plastic cap as applied to a cornea.

SURGICAL PROCEDURE

Preoperatively, an impression is made by the standard technique used in fitting contact lenses. From this an acrylic cap is molded. The cap is cut, using a dental drill and burr, to the proper shape (fig. 10).

The operative steps are the same as for the standard corneal transplantation up to the time of making the trephine scratch. After this, the cap is placed over the corneal area and three preplaced sutures are passed through the cornea, one for each arm of the cap. Any two sutures oppose one another (fig. 11).

The cap is then removed and the operation proceeds in the usual manner, when the

donor graft is in place in the recipient cornea, the sutures are passed through the opening in the cap, the cap is put in place, and the sutures are tied snugly. The cap is removed on the eighth postoperative day.

Summary and Conclusions

Experimental work in developing a satisfactory plastic cap for maintaining a corneal graft in place postoperatively has been presented.

The results of three human cases has been presented.

It is concluded:

1. A plastic cap is a suitable adjunct to corneal grafting.

2. The cap is well tolerated by the cornea without irreversible changes.

3. There is apparently less postoperative edema of the graft with the use of a cap than with sutures.

4. The impression of the cap was not present on the graft in any case and showed no evidence of "cutting into" the graft as sutures do on occasion.

5. There is no impediment to healing with the use of a cap.

6. The cap is easily applied to the cornea and easily removed.

7. There was no delayed reformation of the anterior chamber in any of the cases and no synechias were formed.

8. It is believed that patients with this cap may be more active postoperatively than when sutures are used.

9. There appears to be less photophobia immediately postoperatively and during the convalescence.

10. Further work with the cap should be done and more exacting analyses should be made.

220 Engle Street.

I wish to express my appreciation to Miss Theresa Fennesey, R.N., Miss Ruth Back, Miss Jean Kennedy, R.N., and Miss Dorothy Fuller, R.N., for their assistance.

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PSEUDOGLIOMA*

A clinicopathologic study of 15 cases

Part III. Clinical considerations

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Clinical considerations

The essential point of clinical interest is, of course, that of the diagnosis and the differentiation from retinoblastoma. Some conclusion as to the diagnosis can be gained by a review of the incidence as to age, sex, race, and bilaterality; the history as to the presenting symptoms; the general health of the child and the maternal health; and the examination of the eye as to the external appearance and as to the ophthalmoscopic findings. To a lesser extent the subject of treatment is of interest, both as to the actual treatment and to possible prevention.

* From the Department of Ophthalmology, Washington University School of Medicine, and the Oscar Johnson Institute. Candidate's thesis presented toward membership in the American Ophthalmological Society, accepted by the Committee on Theses. Part I of this paper appeared in the January, 1952, issue of the Journal, pages 61-66; Part II appeared in the February, 1952, issue, pages 199-213.

INCIDENCE

The age incidence is very interesting inasmuch as it can be well correlated with the actual diagnosis.

There were six patients under one year. In this group are listed the cases of retrolental fibroplasia, the case of congenital defect (the persistence of the posterior tunica vasculosa lentis), the case of organized hemorrhage which was considered as a possible birth injury, one of the cases of chorioretinitis, and only one case of exudative retinitis (Case 5), which was the earliest of the whole of this group and is the only one which had not gone on to complete detachment.

In the second year were three cases, two of the active cases of exudative retinitis and one case of chorioretinitis. In the case with cyclitic membrane from vitreous abscess, the patient was four years old. The two patients with massive fibrosis of the retina were a little older, one in the third year and the other, aged seven years, was the oldest in the series. In only one case of the early stage of exudative retinitis was the patient over two years of age, Case 10 in which the age was four years. Both of the late cases of exudative retinitis were in patients in their third year; the condition had probably been present for some time.

The sex incidence shows 10 males and five females. This is interesting in that of the six cases of exudative retinitis only one was a female. This substantiates Coats's original statement that exudative retinitis is predominant in males. Marshall and Michaelson[27] also make this statement for the Leber type.

Except for retrolental fibroplasia, the other conditions do not seem to have any particular relationship to sex. In the series of Owens and Owens,[11] of 10 cases in which they observed the development of retrolental fibroplasia, the sex ratio is seven males to three females. King[70] found in 238 clinical cases of retrolental fibroplasia that 149 (63 percent) were males and only 89 (37 percent) were females. Elsewhere in the literature[71] it has also been stated that the condition is more prevalent in males. This sex incidence also suggests a relationship between exudative retinitis and retrolental fibroplasia.

Of the 15 cases only three were bilateral, one was of retrolental fibroplasia and the other two of possible toxoplasmosis, conditions in which bilaterality is characteristic. In none of our cases of bilateral involvement was the second eye enucleated.

One case of retrolental fibroplasia was that of a Negress (Case 11), the remaining 14 cases were in whites.

CLINICAL HISTORY

In all cases except one, there were very definite presenting complaints or symptoms noted by the parents. Case 12, the unilateral retrolental fibroplasia, was found by examination on admission to the hospital.

These complaints fall in the general classifications of deviation of the eye, mass noted in pupil, apparent loss of vision, and pain with inflammation. One of the prominent complaints is deviation, noted in seven cases. These seven were all unilateral and were usually in older patients. In one case of possible toxoplasmosis the chief symptom was nystagmoid movement.

Poor vision was also noted in seven cases, obviously being in the bilateral cases and in the older children in whom there were subjective complaints. Discoloration of the pupil was surprisingly noted in only five cases, practically all types being represented in which there was a retrolental mass.

Pain and inflammation were prominent in only two, the case of inflammatory cyclitic membrane and the case of active granulomatous chorioretinitis. This, of course, is to be expected as these were the only two active inflammatory conditions.

General health of these children was usually excellent, there being only four in which a statement as to their general condition was noted. In Case 5, the very early case of exudative retinitis, this history is

probably incidental as the disease was a rectal fistula cured by surgery at the age of a few months.

In one case of retrolental fibroplasia (Case 12) the child was almost stuporous and had one convulsion on admission to the hospital. This case was that of a premature and the condition may have been due to the permaturity. As expected, the case of postinflammatory cyclitic membrane did have a history of a long, unexplained fever.

Case 2, a case of late exudative retinitis, was particularly interesting in that there was hemilipodystrophy involving the right side of the head, the right shoulder and arm. This child had been in the hospital one year previously because of this condition. At this time the eye was externally normal, but no ophthalmoscopic finding was noted. This case is also particularly interesting in that there were multiple tumors, one on the scalp being diagnosed histologically as a hemangioma, the other on the arm as a neurofibroma. Any possible significance of these findings is conjectural.

Only two of the cases were in prematures, both of these being retrolental fibroplasias.

In none of these cases was there any history of maternal disease except for the one case of possible toxoplasmosis, in which the mother was supposed to have had a severe cold with no skin eruption during the first trimester of pregnancy. The difficulty of obtaining such a history accurately and the fact that in many of the earlier cases solicitation of such history was not attempted, the absence of findings relative to maternal health is probably not significant.

Ocular examination

In seven of the cases the external examination was completely normal; these represented the two cases of massive retinal fibrosis and five cases of exudative retinitis. These are the cases in which an externally normal eye would be expected. Two of the eyes were actively inflamed, one of them showing a postinflammatory cyclitic membrane, the other, with acute glaucoma, revealed the persistence of the posterior tunica vasculosa lentis.

The remaining six showed definite findings in the anterior segment, such as small cornea, shallow to completely obliterated anterior chamber, atrophy of the iris, and posterior synechia. This group included the two cases of retrolental fibroplasia, the two chorioretinitis cases, and the case of vitreous hemorrhage. In this group also was the case of late exudative retinitis, but it is significant that the other five cases of this condition were completely normal externally.

Three cases had definite elevation of tension; they were those of one of the chorioretinitis patients, of the patient with persistent tunica vasculosa lentis who also had a very definite maldevelopment of the anterior chamber and angle, and of the patient with the old case of exudative retinitis that had a shallow anterior chamber, posterior synechia, and iris atrophy.

Ophthalmoscopic examination, as would be expected, showed a lesion in all cases except one, in which ophthalmoscopic examination was unsatisfactory because of lens opacity. From the clinical records it is impossible to get any detailed description of the fundus and any discussion must be along general lines.

Five cases presented a white mass immediately behind the lens—two exudative retinitis, two retrolental fibroplasias, and one chorioretinitis. A white mass in the vitreous was noted in four, the two cases of cyclitic membrane, one of exudative retinitis, and one case of chorioretinitis. As might be expected, three of the cases of exudative retinitis appeared to have white solid detachments.

The most characteristic fundus picture was in the cases of massive retinal fibrosis; in one case a band of tissue extended obliquely across the fundus, the other had a localized retinal mass extending forward into the vitreous.

Diagnosis

In nine cases the final clinical diagnosis was retinoblastoma. In two (Cases 2 and 15) the diagnosis was pseudoglioma, Case 2 from the appearance of the anterior chamber and Case 15 from the fundus picture. In both cases it was felt that the risk of leaving a questionable globe in place was not worth taking. In four cases (Cases 4, 8, 13, and 14) there was so much doubt, chiefly because of the anterior-segment findings, that a definite clinical diagnosis of either retinoblastoma or pseudoglioma was not made.

The finding of abnormalities in the anterior segment, such as microcornea, iris atrophy, posterior synechia, shallow or collapsed anterior chamber, are, therefore, the most suggestive findings in pseudoglioma. The presence of an active inflammation would also suggest this diagnosis. The presence of a glaucoma is probably not of any significance since many cases of retinoblastoma also have increased tension. The ophthalmoscopic picture, both of retinoblastoma and pseudoglioma, may be so inconstant and lacking in diagnostic characteristics that much of the time it merely puts the case in the category of a suspected tumor.

A history of preceding systemic illness, particularly that which might be a meningitis or some sort of pyogenic infection, would strongly suggest the vitreous abscess with secondary organization of membrane. The clinical picture of persistence of the posterior tunica vasculosa lentis, according to the literature, is usually quite typical, but could be confused with cyclitic membrane.

If the external examination is normal, if the fundus picture suggests a detachment, and if the patient is a very young male, the type of pseudoglioma suggested would surely be that of exudative retinitis. However, in the late cases in which the retina comes in contact with the posterior surface of the lens with a retrolental membrane, the cyclitic membrane type might be simulated.

Although it is evident that most cases of retrolental fibroplasia present a typical clinical appearance, the presence in this series of two atypical cases suggests that these atypical types can be easily confused with other intraocular disease in infants, although, with increasing knowledge of this condition, this is less likely. The presence of prematurity and bilaterality are, of course, very strongly suggestive of retrolental fibroplasia.

An ophthalmoscopic picture of strands and masses extending into the vitreous in an older child with externally normal eyes is suggestive of massive retinal fibrosis.

From the standpoint of diagnosis one of the most interesting facts found in this survey was the very high incidence of pseudoglioma in relationship to retinoblastoma. It was hardly to be expected that, of every five cases removed as retinal tumor, one would be a pseudotumor. There is a practical application of this fact.

When enucleation of a tumor suspect is discussed with the parents, the possibility of inflammatory mass should be mentioned. But it is, of course, emphasized that the chances are very definitely in favor of the tumor being a cancer and that the eye is hopelessly lost.

Under these circumstances, a pathologic diagnosis of one of the types of pseudoglioma brings relief to the parents with regard to the future health of the child rather than doubt as to the necessity of removal and perhaps censure as to mistaken diagnosis which might occur if the possibility of pseudotumor is not mentioned.

From the above discussion it would seem evident that any accurate differential diagnosis from true retinoblastoma in the majority of these conditions is impossible.

Treatment

It is immediately evident that for most cases of this condition there is no treatment other than enucleation. From the pathologic studies, it has been shown that of these 15 eyes all except two were completely and

hopelessly blind, one of them from glaucoma and the rest from complete massive detachment of the retina. Of the two eyes showing massive retinal fibrosis it seems that the lesion is probably progressive and the prognosis is hopeless. Therefore, it can be concluded that from the histologic examination alone, enucleation was justified in all of these cases.

Also from the clinical examination alone in practically all cases, it is impossible to differentiate them absolutely from true retinoblastoma. With the above pathologic findings in mind, it is again obvious that there is no point in attempting to save the globe and that enucleation is almost always indicated. This is particularly true if a mistaken diagnosis of pseudoglioma is made and the eye is allowed to remain in place. There are such cases reported[72, 73] in which this has happened with fatal outcome.

There is only one group of cases in this series in which there is any possibility of treatment. This is the persistence of the posterior tunica vasculosa lentis, the only type in which complete retinal detachment or marked retinal disease is not usually present. If the eye has no other apparent disease, then surgical removal of the fibrous membrane from the posterior surface of the lens can be attempted. This has been described in detail by Reese.[9]

Summary and Conclusions

A series of 15 cases of pseudoglioma, collected over a period of approximately 21 years from a total of 2,056 eyes, is reported. In this particular series, with 169 children, aged seven years and under, the diagnosis of tumor was the reason of enucleation in 45.5 percent. The ratio of pseudoglioma to actual retinoblastoma was 1.0 to 4.1. This series is not only the largest in the literature, but also only the second one to be collected.

Pathologically these pseudogliomas represent seven distinct classifications, all of them found characteristically in children.

Type I. Persistence or hyperplasia of the posterior tunica vasculosa lentis (one case), one of the best recognized types of pseudoglioma, has been well described in many case reports in the literature. Apparently the great majority of these cases are associated with a patent, persisting, hyaloid artery which acts as a feeder vessel to a connective-tissue mass on the posterior surface of the lens.

Type II. Organization of vitreous mass (two cases) has also been well recognized for years and fully described in the literature. The majority of these cases are due to organization of an anterior vitreous abscess which is usually associated with a systemic infection, such as meningitis. However, there are well-recognized cases on a similar basis due to organization of anterior vitreous hemorrhage.

Type III. Chorioretinitis (two cases). From the literature this type is the rarest pseudoglioma, as uveal inflammation of the endogenous type is unusual in children. The cases previously reported are usually massive conglomerate tuberculomas of the choroid.

Although confirmatory evidence, such as identification of the organism, positive serologic test, or positive X-ray findings, has not been obtained, the two cases herein reported may represent toxoplasmic choroiditis.

Type IV. Exudative retinitis (six cases) is the most important type numerically, with four early and two late cases. All these cases are quite similar and apparently represent a definite pathologic picture. This condition seems to be identical with Leber's serofibrinous type of exudative retinitis that has been well described in the literature.

Although the term, exudative retinitis, for this type of disease seems to be accurate and descriptive, it should not be confused with the prevalent idea of Coats's disease as there is pathologically no similarity in these conditions.

The presence of this condition in such a relatively large number of these children suggests that this disease should be better

recognized as a clinical and pathologic entity.

Type V. Massive retinal fibrosis (two cases) represents the type of lesion which has been previously reported only once by Reese,[25] and was given the name in that report of massive retinal fibrosis in children. The two cases here reported seem to be identical with those reported by Reese. However, it is not clear whether the etiologic background of localized hemorrhage in the retina, with subsequent fibrosis, is the same in these two cases as in those previously reported.

Type VI. Retrolental fibroplasia (two cases). Neither of these cases presents the typical picture clinically. Although there are very few cases of this condition reported pathologically, these two cases seem quite similar to those few cases on record. It is doubtful that there is any direct relationship of this condition to persistence of the posterior tunica vasculosa lentis. Inasmuch as both this condition and exudative retinitis seem to be metabolic vascular diseases, there may be some relationship between these two conditions.

Type VII consists of other tumors, such as diktyoma or angiomatosis retinae. This type has no representative case in this series.

The mass observed ophthalmoscopically may be a retrolental membrane, a vitreous mass, a solid opaque retinal detachment, or a localized retinal mass.

The chief point of clinical interest is the differential diagnosis from true retinoblastoma. Of these 15 cases, the final clinical diagnosis was retinoblastoma in nine. In six, the diagnosis was doubtful with the possibility of pseudotumor evident.

After reviewing the incidence, the history, and the physical findings, it was found that abnormal findings in the anterior segment, such as microcornea, iris atrophy, posterior synechia, and shallow or collapsed anterior chamber, were the findings most likely to suggest pseudoglioma. Conversely, the exudative retinitis group is characterized by normal anterior segments and solid-appearing detachments in very young males.

The presenting complaints of deviation of the eyes, loss of vision, and mass in the pupil were of no value in the differential diagnosis. The history of the general health of both the mother and the child was also of no particular value except that, in endophthalmitis cases, there may be a history of febrile disease.

It can be concluded that, from the clinical findings alone, an absolute differential diagnosis for retinoblastoma is usually impossible.

Inasmuch as these eyes are usually hopelessly blind from extreme pathologic changes and as it is usually impossible to differentiate them absolutely from retinoblastoma, enucleation is the indicated treatment in almost all cases.

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LENS-INDUCED UVEITIS AND GLAUCOMA*

Part II. The "Phacotoxic" Reaction

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II. "Phacotoxic" Reactions

(Cases 9 through 11)

In the paper in which Verhoeff originally described endophthalmitis phaco-anaphylactica, he also mentioned cases in which the reaction in the eye "produced by Morgangnian fluid is not a reaction of anaphylaxis but is analogous to that produced by any necrotic tissue."

At that time Verhoeff did not elaborate on this group which is not generally recognized as a pathologic entity, but he expected to do so later, as he stated in a personal communication.

This group consists of cases with hypermature cataract. The lens substance, escaping into the eye cavities, produces uveitis and glaucoma. Pathologically there is: (1) Marked plasma-cell reaction in the iris; (2) if lens material is exuded posteriorly, a marked cyclitis with plasma-cell and mononuclear phagocytic-cell response clouding the vitreous; and (3) the deposition of clumps of cells on the retina and on Descemet's membrane. In contrast to Group I, giant cells and polymorphonuclear cells are relatively inconspicuous.

A typical case follows:

Case 9

October 14, 1937. A 76-year-old woman was seen for the first time with bilateral immature cataracts. Vision was 20/200, O.U.

November 2, 1937. Cataract extraction was performed on the right eye. The capsule was inadvertently broken and a small capsular tag and a slight amount of cortex were left in the anterior chamber. There was no loss of vitreous. Recovery was uneventful until November 18th when the eye became congested. Tension was soft and there was a marked aqueous flare. The capsular remnant was swollen and adherent to the vitreous face where an opacity was developing. The iritis continued. The vitreous face thickened into a membrane.

November 30, 1937. A keratome incision was done and the anterior chamber was irrigated. The capsule could not be removed as it was fused with the vitreous face. Surprisingly little reaction ensued and the patient volunteered that that night was the first she had experienced without pain since the cataract extraction. The eye quieted down promptly.

January 6, 1938. Vision was 20/40.

March 3, 1938. Vision was 20/20 and the vitreous was clearing completely.

June 14, 1938. The patient complained of irritation in the unoperated left eye.

June 22, 1938. Examination revealed ciliary congestion, iris adhered to the lens, O.S. There were keratic precipitates and many cells in the aqueous. The right eye showed no inflammation. The uveitis continued to increase and extremely large, lardaceous precipitates were deposited on the cornea. Secondary glaucoma ensued.

August 2, 1938. Condition was unimproved; aqueous aspirated for cell study revealed many lymphocytes, rare polymorphonuclear cells, and no eosinophils. Keratome incision was then made and iridectomy done. The anterior chamber was irrigated but the keratic precipitates remained fastened to the cornea. The iris specimen showed increased thickness due to infiltration with lymphocytes and plasma cells. There were

* From the Estelle Doheny Eye Foundation Laboratory, Los Angeles, California. Presented before the Western Section of the Association for Research in Ophthalmology, Portland, Oregon, 1950. Part I of this paper appeared in the February 1952 issue of the Journal, pages 177-186.

no epithelioid cells. A diagnosis of sympathetic ophthalmia was not justified.

September 6, 1938. The cornea was literally plastered with lardaceous keratic precipitates. Light perception was faulty; tension was high. There was considerable pain, so enucleation was performed.

Before enucleation, aqueous was withdrawn which showed a total protein of 3,000 mg./100 cc. and numerous cells.[8] There were 84 percent lymphocytes; 16 percent polymorphonuclear cells. The blood sugar was 78 mg. and the aqueous sugar 39 mg. per 100 cc. It is significant that at no time, during the course of inflammation of the left eye, was the right eye inflamed. Sections from the enucleated eye were sent to Dr. Verhoeff for an opinion, and an excerpt from his report follows:

"This is not a case either of sympathetic uveitis or of phaco-anaphylaxis, but the inflammatory reaction is due to toxic lens matter, a reaction that not infrequently occurs in cases of hypermature cataract. The lens in your case is not hypermature from a clinical standpoint, but the cortex, especially posteriorly, has become completely fluid just as in the case of a hypermature cataract.

"At the posterior pole the capsule shows solution of continuity and lens matter can be seen in the vitreous here. Numerous eosinophilic balls of various sizes can be seen here which you may have mistaken for blood corpuscles. Of course these balls represent only a small portion of the lens matter which had been given off into the vitreous.

"The reaction is typical, consisting chiefly in exudation of macrophages. There are masses of these in the anterior chamber and nodules of them on the surface of the retina. The almost complete absence of pus cells shows that it is not a phaco-anaphylactic reaction.

"The iris, both in the eye and in the piece that you removed by iridectomy, shows chiefly plasma-cell infiltration.

"In your note you state, 'The lens cortex was completely broken down, giving a milky appearance.' If you could have made the diagnosis early and removed the lens, this eye no doubt could have been saved. . . .

"I am planning some time to write up this condition. I have a number of eyes (with hypermature cataract) showing it. Many eyes have been lost from it which would have been saved if the lens had been removed instead of the eye."

Description of pathologic anatomy

Microscopically, the basal epithelium of the cornea is swollen and edematous, whereas the overlying stratified layers appear to be compressed. There is an abnormally sharp transition between these two types of epithelium, and the cell layers appear to be somewhat reduced in number.

The limbal episclera is densely infiltrated with lymphocytes and plasma cells as far posteriorly as the plane of the ora serrata. These cells infiltrate the stroma anteriorly and peripherally.

A few dilated blood vessels are seen extending from beneath Bowman's membrane at its periphery. Nasally, there is a free collection of blood separating the epithelium from the underlying Bowman's membrane, from the limbus to the center of the section. The endothelium is somewhat flattened and attenuated centrally.

The anterior chamber is shallow and nearly filled with an inflammatory exudate. There are large focal accumulations of pale-staining cells having oval to sickle-shaped nuclei with distinctly staining chromatin material and single or multiple nucleoli.

These cells have an abundant cytoplasm and have a strong tendency to adhere to one another, thereby forming large precipitates on the posterior cornea and anterior surface of the iris. It is noteworthy that the nuclei resemble those of epithelioid cells, as well as those of mononuclear macrophages.

There is also a small amount of free blood throughout the anterior chamber. Polymorphonuclear leukocytes and occasionally

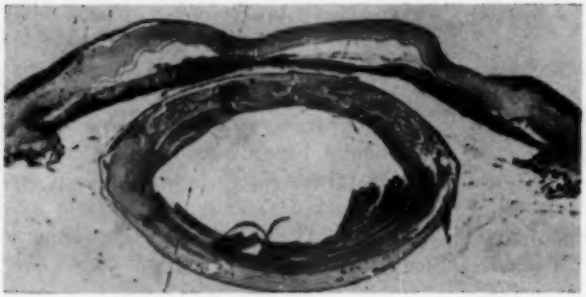

Fig. 6 (Irvine and Irvine). *Case 9.* Anterior segment, showing marked inflammatory infiltration of iris and anterior chamber.

eosinophilic leukocytes are seen. Small peripheral anterior synechias appear to be formed by interspersion of macrophages and chronic inflammatory cells between the trabecular meshwork and the iris root.

The iris is heavily infiltrated by plasma cells, partially destroying its normal architecture. There is a collection of free blood between the dilator muscle and the pigment epithelium in the temporal leaf centrally. There is some atrophy of the pigment epithelium, particularly in its pupillary portion. An organized inflammatory exudate consisting primarily of lymphocytes, plasma cells, and pigment-laden mononuclear phagocytes, but also containing necrotic polymorphonuclear leukocytes, extends across the pupillary space. Macrophages and a few polymorphonuclear leukocytes are seen along the anterior surface of the lens.

The ciliary body shows less chronic inflammatory change than the iris. Macrophages similar to those seen in the anterior chamber are evident between the ciliary processes and appear to originate from them. These cells are seen in the circumlental space, in the anterior vitreous, along the internal limiting membrane of the retina posteriorly, and lining the optic cup.

The lens cortex is liquefied and shows extensive globule formation. The epithelium is diminished anteriorly and equatorially. Posteriorly the demarcation of the capsule is difficult to discern. Small globules of lens material are seen outside the capsule in the posterior lental space and in the anterior vitreous.

The choroid, except for a few scattered foci of lymphocytes, is free from inflammation.

There is a collection of free blood in the nerve-fiber layer of the retina, temporally, half way between the equator and nervehead. Lymphocytes are seen perivascularly in the nerve-fiber layer. Ganglion cells are plentiful, and there is no atrophy of the nerve-fiber layer or of the nerve trunk.

Impression. Hypermature cataract. Lens-induced iridocyclitis (toxic response).

Comment. Many of the phagocytes within the anterior chamber have nuclear characteristics indistinguishable from those of epithelioid cells. The pink-staining cytoplasm and the presence of brown pigment granules in many of the cells confirm their phagocytic activity.

Typical epithelioid cells, occurring in nodules, and aggregating to form giant cells are not seen. For this reason a diagnosis of chronic granulomatous inflammation is not justified. However, the similarity of the nuclei of these mononuclear phagocytes and the nuclei of epithelioid cells suggests their common origin.

Comment on Group II

In retrospect, the clinical diagnostic features of Case 9 seem to be the presence of a mature to hypermature lens; extremely-high protein content of the aqueous, part of which must have come from the lens; and the covering of the back of the cornea with large, irregular, lardaceous precipitates.

The time of onset after cataract extraction

would suggest sympathetic ophthalmia. The fact that the opposite eye was never inflamed was, however, definitely against this diagnosis. A review of 63 cases of sympathetic ophthalmia[18] revealed that exacerbations of attacks were bilateral when both eyes were present.

Details of two other cases included in this group (Cases 10 and 11) are appended. Probably some of the cases that are reported as having been cured by removal of the lens would have fallen into this group had the condition been allowed to progress.

Pathologically, the anterior segment is involved primarily. The extreme plasma-cell infiltration of the iris and the presence of lens material in the vitreous and aqueous, being phagocytized by large eosinophilic-staining macrophages, identifies this group.

There may be, in addition, a slight polymorphonuclear response, showing an overlapping of Groups I and II. The polymorphonuclear cells do not seem to indicate the acuteness of the process, as the example Case 1 in Group I showed polymorphonuclear infiltration in an eye that had been affected for approximately one year.

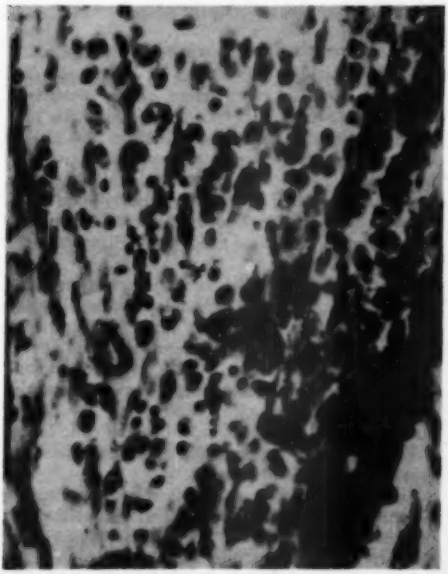

Fig. 7 (Irvine and Irvine). *Case 9.* Exudate in anterior chamber and iris, showing predominance of plasma cells.

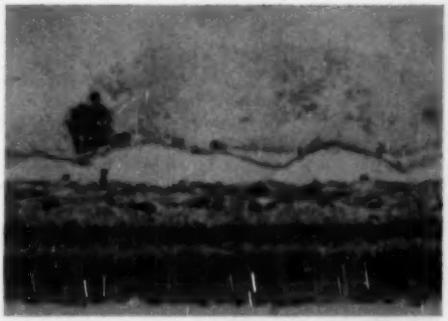

Fig. 8 (Irvine and Irvine). *Case 9.* Cells clumped on retina, similar to collections seen as keratic precipitates.

In Group II, the overall picture is that of predominant mononuclear-cell infiltration, whereas in Group I there was predominance of polymorphonuclear and giant cells. There is, however, no sharply defined pathologic distinction, and perhaps both Groups I and II might be classified together as Straub's[19] "endophthalmitis phacogenetica," or lens-induced uveitis, until the etiology (of anaphylaxis or lens toxicity) is established by more absolute criteria.

Synopses of cases in Group II*

Case 10

May, 1948. A man, aged 75 years, had a glaucoma operation on the left eye. The eye was irritable, with many keratic precipitates.

November 30, 1948. The right eye became congested and, since sympathetic ophthalmia was feared, the left eye was enucleated.

Description of pathologic anatomy

At the upper limbus is a grayish brown ridge of tissue four-mm. wide, confluent with the cornea and containing in its center a two-mm. dark spot which has the gross appearance of a trephine opening.

The shallow anterior chamber contains a funnel-shaped exudate, the apex of which extends to the opening noted above. The pupil did not transilluminate light.

* For pathologic examination all specimens, unless otherwise specified, were fixed in formalin Zenkers, embedded in celloidin, and stained with hematoxylin and eosin. Gross descriptions, recorded when the eyes were opened, are omitted unless pertinent.

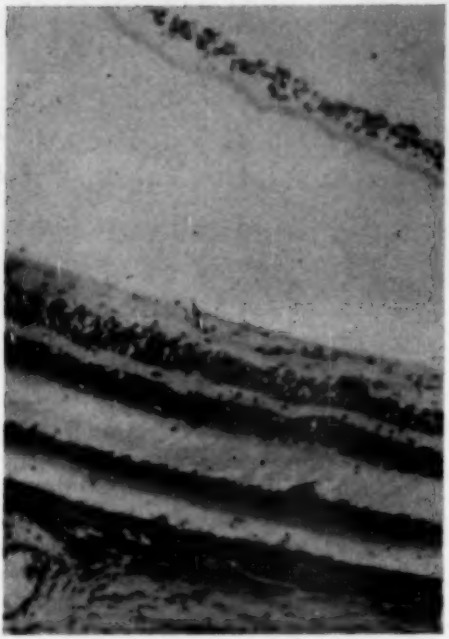

Fig. 9 (Irvine and Irvine). *Case 9.* Normal retina with preservation of ganglion cells.

The corneal epithelium is irregularly thinned and attenuated. Centrally it is reduced to two to three cell layers in thickness. The episcleral connective tissue is injected and its stroma is heavily infiltrated with lymphocytes and plasma cells.

A few small blood vessels are seen beneath Bowman's membrane at its extreme periphery. There are chronic inflammatory cells in the anterior stroma peripherally. The endothelium is flattened, attenuated, and in places is not visible.

The anterior chamber contains serum, polymorphonuclear leukocytes, eosinophilic leukocytes, and mononuclear inflammatory cells. Broad peripheral synechias occlude the trabecular meshwork and extend about three mm. anteriorly on each side. A dense inflammatory exudate composed primarily of polymorphonuclear neutrophilic leukocytes fills the pupillary space, the posterior chamber, and circumlental space as far as the equator, and extends over the corona ciliaris and pars plana, and gradually terminates in the area of the ora serrata.

The architecture of the pigment epithelium of the iris is modified by marked infiltration with plasma cells and lymphocytes. In places the pigment epithelium, both of the iris and of the ciliary processes, shows nearly complete dissolution. Plasma cells are in the anterior vitreous and circumlental space, apparently arising from the ciliary body.

The choroid is distended by serum and plasma cells anteriorly, but is otherwise normal except for occasional lymphocytic foci posteriorly.

The retina shows foci of edema of the nerve-fiber layer, near the macula. The nerve-fiber layer is diffusely infiltrated by lymphocytes and plasma cells, the former perivascularly. The ganglion cells are diminished, and glial elements are increased, particularly in the nerve-fiber layer as it approaches the optic cup, and in the optic nerve. A similar lymphocytic infiltration is seen around the vessels of the optic nerve at the disc.

Aggregates of mononuclear cells are seen along the internal limiting membrane of the retina, and lining the optic cup. These nodules sometimes measure 0.5 mm. in diameter and are composed primarily of large slightly eosinophilic mononuclear phagocytes and plasma cells. There is no evidence of granulomatous uveitis.

Opinion. Exogenous septic endophthalmitis. Hypermature cataract. Lens-induced uveitis (toxic response).

Comment. The heavy plasma-cell infiltration of the anterior uvea in the presence of a hypermature cataract suggests the factor of reaction to toxins from the lens.

CASE 11

September 30, 1948. A right eye sustained contusion injury and rupture of the cornea. Repair of cornea resulted in posttraumatic inflammation which subsided.

February, 1949. There was a recurrence of inflammation and the eye was enucleated. There is no information available about the opposite eye.

Description of pathologic anatomy

Microscopically, the cornea is thickened and edematous and is vascularized at its periphery. There is a healed penetrating wound three mm. inside the limbus nasally. Lymphocytes and plasma cells are seen in the episcleral connective tissue at the limbus. The stroma is thickened and edematous.

The nasal iris leaf is folded anteriorly upon itself, and its pupillary portion is incarcerated in the limbal wound. This leaf blocks the chamber angle nasally.

There is a small peripheral anterior synechia temporally, loosely attached and partially obstructing the trabecular meshwork. The iris stroma is densely infiltrated with lymphocytes and plasma cells. "Clump cells" are seen, and the pigment epithelium is atrophied. Amorphous debris containing scattered mononuclear phagocytes, chronic inflammatory cells, and occasional eosinophilic leukocytes is seen in the anterior chamber. No large aggregates of cells are noted.

An organized inflammatory membrane, consisting of liquefied cortex, capsule, swollen lens epithelium, and inflammatory tissue, bridges the ciliary body laterally, and attaches to the temporal iris leaf anteriorly, thus occluding and secluding the pupil. The

cortex is invaded by mononuclear phagocytes, ladened with cortex, plasma cells, lymphocytes, and foreign-body giant cells.

A newly formed connective tissue, probably representing epithelial metaplasia, is seen on the anterior surface of the lens remnant, between it and the iris leaf. Chronic inflammatory cells, phagocytes carrying lens material, pigment, and cellular debris are noted about the pupillary membrane. A few eosinophilic leukocytes are evident.

There is mild chronic inflammation in the ciliary body. The choroid is distended, and contains occasional small nests of lymphocytes. There is a serous separation of the choroid and ciliary body temporally, and anteriorly.

The retina is separated from the disc to the ora serrata. Its layers are edematous. Ganglion cells are plentiful. Lymphocytes are seen around the vessels of the nerve-fiber layer. The vitreous cavity is filled with an eosinophilic coagulum sparsely infiltrated with chronic inflammatory cells and mononuclear phagocytes.

Opinion. Penetrating wound of the eyeball; hypermature traumatic cataract; traumatic separation of the retina; lens-induced uveitis (toxic response).

Comment. There is no evidence of chronic granulomatous uveitis. This case has features of both endophthalmitis phaco-anaphylactica and the so-called toxic response, and illustrates the overlapping of these groups. It is placed in Group II because of the hypermaturity of the lens.

(To be concluded)

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19. Straub: Amsterdam, 1919. Reviewed by Gifford, S. R.: J.A.M.A., **85**:351, 1925.

THE RESPONSE OF THE RETINAL VESSELS TO PRISCOLINE IN DIABETES MELLITUS*

Study II

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Introduction

In several earlier reports, the action of priscoline as a general vasodilatory agent has been described. In smaller doses it has a histaminelike action on the blood vessels; in larger concentrations it blocks adrenergic responses. Various workers have also proved this effect on the retinal arteries.

It has long been argued that the vessels of diabetics tend to reveal early arteriosclerotic changes, especially in the extremities. This is the explanation given in many standard texts as the cause of the commonly noted vascular complications in diabetics. Various authors have assumed that since diabetic retinopathy occurs with arteriosclerosis, it is the sclerosis which is the basic cause of the onset of hemorrhages, exudates, and aneurysms in the retina.

Waite and Beetham[1] have revealed that, under 30 years of age, 92 percent of diabetics had no evidence of retinal sclerosis. However, between 40 and 49 years of age, only nine percent disclosed this finding. They state that retinal hemorrhages in diabetics multiply with age and duration of the disease, and show no obvious correlation with retinal sclerosis.

Elwyn[2] believes that, because diabetes occurs most frequently in persons past middle age, the normal signs of aging of the vessels are often interpreted as arteriosclerosis.

Friedenwald[3] has recently stated that diabetic retinopathy is not an atherosclerotic manifestation. The vascular lesion, he adds, which results in retinopathy is specifically related to the metabolic disturbance of the dia-

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betic. Appel[4] also reports that vascular changes depend upon the duration of the disease. In a large study of diabetics, he found that 70 percent of all diabetics below the age of 40 years, who have had diabetes over 20 years, have arteriosclerosis.

The incidence of diabetic retinopathy in juvenile diabetics, who have survived 20 years of the condition, has been found to lie between 92 percent and 100 percent, by Dolger,[5] White,[6] Chute,[7] and Joslin.[8]

Fatal coronary sclerosis in diabetics has been reported to be twice that of nondiabetics in a survey conducted by Root, Bland, Gordon, and White.[8] These studies tend to emphasize the statement of Dry and Hines,[9] that a factor contributing to the onset of arteriosclerosis is diabetes mellitus.

A previous report[10] has described the response of the retinal vessels in various stages of arteriosclerosis to priscoline by the method of angioscotometry. In continuing with this technique it was decided to evaluate the effect of this drug upon the retinal vessels in diabetes, both with and without diabetic retinal changes.

Method and Material

a. Technique

The technique employed was similar to that described in our previous study.[10]

b. Subjects

Twenty-seven diabetics, with ages varying from 18 to 69 years, were studied at the Long Island College Hospital. The duration of diabetes varied from six months to 30 years. Typical diabetic retinal exudates were manifested in 12 of these cases, with or without other signs of diabetic retinopathy. The remaining 15 patients revealed no exudates, although there were other signs of diabetic retinopathy in some.

c. Procedure

As described in a previous study[10] on retinal vessels in vascular diseases.

The time interval for the maximum effect was about 13 to 18 minutes following the in-

TABLE 1

Diabetics with fair widening response following priscoline injection

Name	Age	Sex	Duration of Diabetes	Control of Diabetes	Funduscopy
	(years)		(years)		
M. S.	81	F	5	Good	O.D. Mild sclerosis of retinal vessels O.S. Mild sclerosis of retinal vessels Few punctate aneurysms between disc and macula
C. F.	61	F	14	Good	O.D. Several punctate aneurysms in perimacular and temporal region O.S. Two punctate aneurysms in upper temporal quadrant
S. M.	69	F	12	Good	O.D. Mild sclerosis of retinal vessels with increased tortuosity Several punctate aneurysms in perimacular region O.S. Mild sclerosis of retinal vessels with increased tortuosity Two punctate aneurysms in perimacular region Two flame-shaped hemorrhages in periphery and one flame-shaped hemorrhage near disc
A. H.	56	M	7	Good	None
E. B.	31	M	8	Poor	O.D. Three punctate aneurysms in periphery O.S. Negative

TABLE 2

DIABETICS WITH GOOD WIDENING RESPONSE FOLLOWING PRISCOLINE INJECTION

Name	Age	Sex	Duration of Diabetes	Control of Diabetes	Funduscopy
N. R.	(years) 54	F	7 years	Good	O.U. Several punctate aneurysms in perimacular region O.S. Two punctate aneurysms in temporal periphery
M. A.	52	M	5 years	Good	O.D. Mild sclerosis of retinal vessels Several punctate aneurysms in perimacular region Few small hard-white, well-defined exudates in perimacular region O.S. Same as O.D. with several aneurysms in periphery
C. T.	63	M	10 years	Poor	O.U. Early macular sclerosis of lens O.D. Two small perimacular punctate aneurysms O.S. One small perimacular punctate aneurysm
H. S.	18½	F	3 years	Good	O.D. Three punctate aneurysms in perimacular region and two in periphery O.S. One punctate aneurysm in perimacular region
J. W.	51	M		Good	Negative
A. I.	54	M	19 years	Good	O.U. Multiple punctate aneurysms in macular region and periphery
J. M.	66	M		Poor	O.U. Multiple punctate aneurysms in perimacular region and periphery
J. D.	25	M	1 month	Good	Negative
Y. F.	53	F		Good	O.U. Mild sclerosis of retinal vessels with some increase in tortuosity of vessels
L. H.	51	M	3 weeks	Good	Negative
A. S.	61	M	6 years	Good	O.U. Mild sclerosis of vessels

jection. The maintenance of maximum dilatation varied from 17 to 25 minutes.

OBSERVATION

Of the 27 diabetics, 12 patients revealed a *poor* widening of the angioscotoma after an injection of priscoline. In 11 of these cases, funduscopy showed the waxy white, well-defined exudates considered typical of diabetes; while in the remaining patient of this group, no exudates were noted.

Ten patients manifested a *good* widening of the angioscotoma. Of these, nine did not reveal any exudates, whereas in one case, some small diabetic exudates were found.

In the remaining five cases with no evidence of exudates, a *fair* widening of the angioscotoma was recorded (tables 1, 2, and 3).

COMMENT

Many theories have been presented concerning the pathogenesis of diabetic exudates. It is believed by Elwyn[8] that, in some diabetics, the exudate is due to a chronic state of subnutrition produced by stasis in the terminal vessels, which leads to deficient oxygen supply, with consequent appearance of hyaline and lipoid bodies.

TABLE 3

DIABETICS WITH POOR WIDENING RESPONSE FOLLOWING PRISCOLINE INJECTION

Name	Age	Sex	Duration of Diabetes	Control of Diabetes	Funduscopy
V. F.	(years) 56	M	(years) 68	Good	O.U. Multiple perimacular waxy well-defined exudates; punctate aneurysm in perimacular region and periphery O.D. Two small flame-shaped hemorrhages between disc and macula
E. U.	40	F	20	Good	O.D. Three small punctate aneurysms in perimacular and temporal regions O.S. Two small whitish well-defined exudates in perimacular region One small aneurysm in periphery
T. C.	57	F	6	Good	O.U. Multiple waxy exudates in perimacular region and several in periphery Several small perimacular aneurysms O.S. Two flame-shaped hemorrhages in temporal region
R. H.	54	F	3	Good	O.U. Multiple whitish well-defined exudates in macular and perimacular region Several drusen in periphery
M. A.	38	F	20	Good	O.D. Multiple whitish yellow well-defined exudates in perimacular region O.S. Multiple waxy well-defined exudates in perimacular region Several small aneurysms in periphery
I. G.	46	F	15	Good	O.D. One waxy well-defined exudate in perimacular region Two small aneurysms in periphery O.S. One waxy well-defined exudate in perimacular region
M. G.	44	M	1	Good	O.U. Moderate retinal arterial sclerosis with increased tortuosity of vessels O.D. Several punctate aneurysms in perimacular region *No exudates or hemorrhages*
W. W.	68	M		Good	O.U. Moderate sclerosis of vessels of retina Marked tortuosity of veins with some varices O.D. Moderate sclerosis of vessels of retina Multiple small aneurysms in perimacular region O.S. Two small waxy well-defined exudates in perimacular region
B. B.	66	F	12	Good	O.U. Moderate retinal arterial sclerosis with marked tortuosity of vessels O.D. Multiple small waxy well-defined exudates in macular and perimacular region O.S. Multiple small waxy whitish well-defined exudates in perimacular region
E. M.	60	F	7	Good	O.U. Mild sclerosis of retinal vessels; no tortuosity O.D. Two waxy well-defined exudates in permacular region Multiple aneurysms in macular region and periphery O.S. Multiple small waxy well-defined exudates in perimacular region and periphery Two flame-shaped hemorrhages near disc

TABLE 3—*Continued*

Name	Age	Sex	Duration of Diabetes	Control of Diabetes	Funduscopy
A. S.	(years) 39	F	(years) 14	Good	O.D. Two small waxy well-defined exudates in perimacular region O.S. Four waxy yellowish well-defined exudates in perimacular and temporal regions Several small aneurysms in periphery
S. A.	61	F	12	Good	O.D. Multiple waxy well-defined exudates in perimacular region Several punctate aneurysms in perimacular and temporal region One flame-shaped hemorrhage superior to macula O.S. Several waxy whitish well-defined exudates in perimacular region

O'Brien and Allen,[11] in an extensive study of diabetes, invariably found arteriosclerosis of the retinal vessels, not only clinically, but also in microscopic observations.

Leopold,[12] however, stated that arteriosclerosis, hypertension, and hyperglycemia may influence the incidence of the waxy exudate, but that no one of these is the basic etiologic factor.

Another theory postulated by Dry and Hines[9] is that diabetes injures the finer arterioles and venules and that this sets the stage for progressive degenerative lesions of the retina.

In this study, 11 out of 12 patients, with no widening of the angioscotoma after priscoline was given intravenously, were found to have diabetic exudates. A previous report[10] has revealed a similar poor widening response to priscoline in patients with marked arteriosclerosis. It is, therefore, believed that possibly the presence of exudates in the retina in diabetics is a manifestation of advanced vascular damage.

From this study, it also appears that the presence of exudates offers the poorest prognosis insofar as the regional retinal vessels and surrounding retinal areas are concerned.

It is also felt that, perhaps, the present diagnostic label of diabetic retinopathy is too broad. It is utilized whenever an aneurysm, hemmorhage, or exudate, alone or combined, is present, and these findings should be more specifically classified.

Conclusion

In 27 cases of diabetes, the response to intravenous priscoline, as noted by its effect upon the angioscotoma, was:

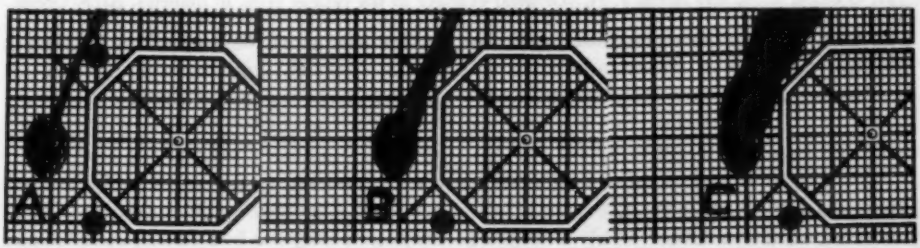

Fig. 1 (Cholst, Schilback, Handelsman, and Levitt). Angioscotoma plotted to show the effect of priscoline in a patient (J. W., Table 2) without diabetic exudates. (A) Normal angioscotoma before priscoline. (B) Four minutes after injection of priscoline. (C) Sixteen minutes after injection of priscoline. (Classified as a *good* response.)

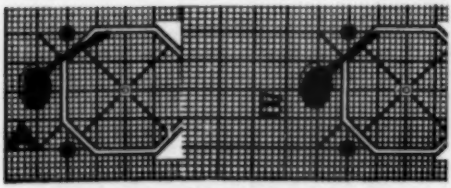

Fig. 2 (Cholst, Schilback, Handelsman, and Levitt). Angioscotoma plotted to show the effect of priscoline in a patient (A. S., Table 3) with diabetic exudates. (A) Normal angioscotoma before priscoline. (B) Fifteen minutes after the injection of priscoline. (Classified as a *poor* response.)

Twelve cases responded poorly. No evidence of widening of the angioscotoma was noted. Of this group, 11 showed typical diabetic retinal exudates, while one remaining case revealed no evidence of diabetic retinal changes (fig. 2).

Five cases indicated a fair response. All of these patients showed no evidence of exudates.

Ten cases revealed a good response. In nine of these, no retinal exudates were found; whereas, in one case in this group, several diabetic exudates, typical but very small, were noted (fig. 1).

The poor response to priscoline in the cases with exudates is analogous to the poor response found in patients with advanced visible arteriosclerosis.

Several patients in the poor-response group were appreciably younger than those found in the accepted "arteriosclerotic age group."

A more descriptive classification of each sign of diabetic retinopathy is recommended. The onset of exudates in a diabetic appears to offer the poorest prognosis.

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NOTE: Cases with any questionable evidence of optic-nerve involvement due to diabetes were excluded from this study.

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CHOICE OF TEST OBJECTS IN VISUAL FIELD STUDIES*

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When studying a patient's visual fields, it is not enough merely to indicate a loss for one particular visual angle. For example, to say that a patient has a temporal hemianopia for 3/330 white does not qualify the extent of defect beyond just that point. It does not tell us if the field is present or absent for 5/330 white, or 10/330 white, or even for hand movements. On the other hand, while the nasal half of this field is shown to be intact for 3/330 white, we do not know if it is still present for 2/330 white or 1/330 white. In other words, the use of a single test object tells neither the depth of loss in the defective area nor the exact quality of the preserved area.

Technically, one might do a series of field studies, using all stimuli, from gross hand movements to 100/330 white, 40/330 white, and so forth, all the way down to 0.5/2,000 white. Certainly, such a complete routine would be time-consuming and entail a good deal of unnecessary recording that would not be worth the effort. Furthermore, the recording of much unnecessary data would detract from proper concentration on the more pertinent critical test that would bring out the quality of the field to be studied.

How does one go about choosing the proper stimuli for a particular field study? Some perimetrists have attempted to lay down rules of thumb for the choice of test objects. I have seen such attempts based on the central visual acuity (Snellen) alone. This is regrettable, because such central visual acuity is an indication of innermost central field only, probably within 0.5 degree from fixation. Visual acuity has been shown to fall off about 20 percent at 0.5 degree and about 30 percent at 1.0 degree from fixation by Weymouth and others.[1]

Involvement within the inner 0.5 degree of field would, therefore, impair central visual acuity appreciably but, at the same time, the surrounding field for such small stimuli as 1/2,000 white may be perfectly intact and the peripheral field intact for such small stimuli as 1/330 white.

When there are no obvious gross defects, such as with hand movements, and a large test object such as 5/330 white is seen in the periphery, one should resort to minimal stimuli in order to look for minimal defects in the various portions of the field.

In speaking of minimal stimuli, we refer to the smallest white test object against a black background, under standard lighting conditions of seven foot-candles, so that it is just made out in the particular area of field which is being explored. Therefore, a single test object cannot be used to explore the entire field, since a stimulus that is minimal at the periphery is no longer minimal in a more central area of the field.

Theoretically, by using fine gradations of test-object size, one could use a different stimulus for every 10 degrees or so of arc. However, such fine division is unnecessary and may even confuse the examiner and fatigue the patient.

On the other hand, individual testing of the various portions of the field is necessary because of the frequency of the involvement of only one portion of field and not the others. For example, in optic neuritis one may find a defect only in the cecocentral area and not more peripherally.

Chiasmal interference may, however, show involvement only in the 10-degree to 25-degree area with the more central and more peripheral fields intact. Finally, in brain tumor or vascular accidents, one may find involvement only in the periphery and not extending more centrally than the 30-degree or 40-degree arcs.

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For practical purposes, therefore, we have found it most convenient to divide the field into central (0 to 10 degrees), intermediate (10 to 25 degrees), and peripheral (25 to 90 degrees).

Minimal testing of the peripheral field

The smallest visual angle said to be just visible in the extreme temporal periphery is believed to be about 0.86 degrees, corresponding to 5/330 white.

While this may be true for elderly or debilitated people, in most healthy people the stimulus formed by 3/330 white is normally visible near enough to the extreme periphery to consider it as a minimal stimulus for testing of the temporal periphery for practical purposes. From a practical point of view, we have found the 2/330 white even more desirable for minimal testing at the periphery, less dense defects being more easily picked up with this lesser stimulus.

True, the temporal periphery for 2/330 white may not extend quite as far out as that for 3/330 white, but it usually extends far out enough to show a contraction due to a tumor or a vascular accident, however peripheral the effect of the lesion. Thus, if the field for 2/330 white reaches to its normal limit in a good part of the periphery, but not in another, one may assume that there is a peripheral defect in the latter area.

On the other hand, if a 2/330 test discloses a field that is normal in contour but does not reach further out than, for example, 45 degrees nasally or 65 degrees temporally, one may assume that the patient has a low normal field for this test object, because a truly pathologic contraction is not likely to produce a field of normal contour and proportionate contraction all around. In such a case it is wise, therefore, to use a 3/330 or even 5/330 to study the remaining periphery of the field. Such a portion of field may be affected in disease of the extreme periphery of the retina.

In order to gauge whether a field reaches out to the normal extent for a particular test object, we use a chart showing minimal normals for 5/330, 3/330, and 1/330. This chart was described in a previous work.[2]

While extremely peripheral defects due to suprageniculate interference have been described (so that only the unpaired portion of the temporal field is affected, and such defect is theoretically possible), it has been our experience that a peripheral defect such as this will usually show some defect in the homonymous nasal field, if one uses a 2/330 or 1/330 white and the minimal techniques and criteria, such as level differences, qualitative differences, and breadth of field differences, described in a previous paper.[3]

Minimal testing in the intermediate field

The intermediate field was suggested as a name for the area between 10 to 25 degrees in a previous study.[4] In that work, it was shown that this area of field was particularly vulnerable to mass interference at the chiasm, which often will cause a great deal of typical chiasmal field defect in the intermediate field with little to no defect in the peripheral field for 2/330 white or even 1/330 white (fig. 1).

Minimal testing in the intermediate field is done with 1/2,000 white, the periphery for which lies between 10 degrees and 25 degrees, depending on the individual. Thus, testing with 2/330 white or 1/330 white only may well lead to a complete oversight of a typical bitemporal hemianopia in the 1/2,000 white field.

Minimal testing of the central field

In testing the central field of vision, the 1/2,000 white can again be used all the way down to fixation. However, in the inner three or four degrees, 1/2,000 white is no longer a minimal test, and one may have to resort to 0.5/2,000 white to pick up tiny defects which should be used when central visual acuity is definitely diminished and the 1/2,000 white field seems to be intact all the way to fixation.

At this point, it is well to remember that *any appreciable loss of central visual acuity (Snellen) in the absence of pathologic change in the media or fundus should be demonstrable by a field defect involving the fixation area.* One must also remember, however, that central visual acuity (Snellen) depends on the function of the innermost central area, probably the inner 0.5 degree, so that defects may encroach very intimately upon fixation without interfering with visual acuity (Snellen).

Of the various colored test objects used in the central area, red seems to be the most useful. For exact quantitative measurements, however, small white test objects are more desirable.[4]

In summary, before reporting fields as normal, the periphery must be shown to be intact for 5/330, 3/330, 2/330, or 1/330 white, depending on the individual. The intermediate field must be shown to be normal for 1/2,000 white, and the central field for 1/2,000 white and 0.5/2,000 white. In addition, central visual acuity must be intact (Snellen). The use of such visual angles will allow almost no defect to escape detection.

Defective field

When there is loss of field, one must qualify it by explaining exactly how intense the loss is. This is most important from a diagnostic as well as a prognostic point of view. Furthermore, it serves as a basis for gauging improvement or greater involvement.

If a loss is a very profound one, even for hand movements, the field chart should be so labeled. On the contrary, if hand movements are still seen, one should flash a 100/330, 40/330, then a 20/330 white, and so forth, until he finds the smallest test object that can just be seen.

Once the quality is thus ascertained in the defective part of the field, the better part of the field is further explored with smaller and smaller stimuli, until minimal stimuli are reached. In speaking of good and defective portions of field, I refer especially to hemianopic defects—homonymous and bitemporal.

Conversely, if minimal stimuli are used in good fields first, the defective portion of the field is examined with larger and larger visual stimuli until the smallest stimulus just visible there is found. Thus, if there is an intact nasal field for 1/330 white, but a temporal hemianopia with this test object, a 2-mm., then 3-mm., then 5-mm. white test object is used until the smallest one that begins to be visible in the defective field is found.

In order to do this, one should indicate on the chart at what point the critical size test object becomes visible. Furthermore, it is very simple and informative to divide the field into upper and lower halves for this purpose. For example, let us assume that a patient has a temporal hemianopia in the right eye for 1/330 white. We are faced with a defective temporal field for evaluation.

In rapid succession 2, 3, and 5-mm. white test objects are flashed in the upper and lower temporal field, well within the normal periphery. Suppose the 2-mm. and 3-mm. objects are not visualized, but the 5-mm. one is just seen. In such case, one should bring the 5-mm. test object along the 45-degree meridian and the 315-degree meridian.

Let us assume that the patient first saw the 5-mm. test object at the seven-degree arc on the 45-degree meridian, and below on the 10-degree arc on the 315-degree meridian.

One should indicate such recognition by a visible dot at the appropriate point, and place the number to indicate the size of the test object, assuming color and distance to be the same as those of the test object used for the better half of the plotted field, unless otherwise indicated. Such a case is shown in the right field of Figure 2. The dot indicates the point at which it is first seen.

By having all the test objects available and within easy reach, the examiner can readily take four or more of them in his hands at one time and flash them in rapid succession. With some experience, he can determine such

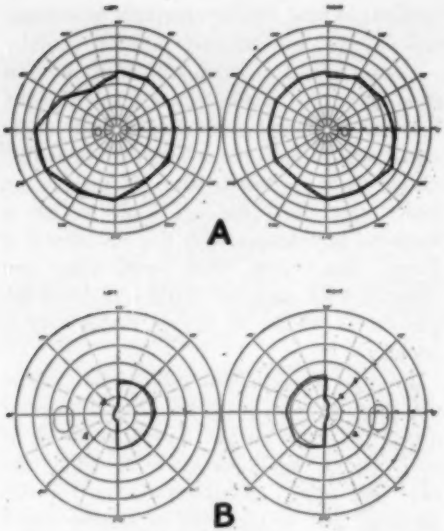


Fig. 1 (Chamlin and Davidoff). M. D. Case of pituitary tumor being treated with radiotherapy. Vision: O.U., 20/30—1. (A) 2/330 white. (B) 1/2,000 white.

findings as the ones just described in a very short time.

In the same case (fig. 2), it will be noted that hand movements were first seen at 20 degrees above and 25 degrees below, thus designating the quality of the intermediate field.

One should go on and in a similar manner find the quality of the peripheral field—for example, between 40 and 60 degrees, and even more peripherally. Since hand movements are not indicated until 20 degrees above and 25 degrees below, this means that not even gross hand movements were seen at the periphery. If desired, one may indicate the absence of the detection of hand movements by inserting "no H.M."

Actually, these four temporal readings, which should take the experienced perimetrist no more than a minute or two to determine, will give a much more accurate record from which to gauge future progress.

Another illustration of the quality of defective field in various areas is shown in Figure 3. For example, in the left field, there is a temporal hemianopia for 2/330 white. However, in the peripheral field, hand movements are seen at 30 degrees in the 135-degree meridian, at 60 degrees in the 180-degree meridian, and at 60 degrees in the 225-degree meridian. At 10 degrees, temporally, the innermost portion of the intermediate field, hand movements are no longer seen. In the nasal field, it is noted that the 1/2,000 field is very small, but the 2/2,000 white is visible at 13 degrees above and 15 degrees below.

In testing the intermediate field on the tangent screen, when there is a contraction with minimal testing or 1/2,000 white, the defective field should again be qualified. For example, if there is a temporal hemianopia for 1/2,000 white, one may use a 2/2,000 white in the defective temporal field, and, if this is not seen, a 3-mm., 5-mm., and so forth, up to hand movements.

Let us suppose that a patient has a right temporal hemianopia for 1/2,000 white, but

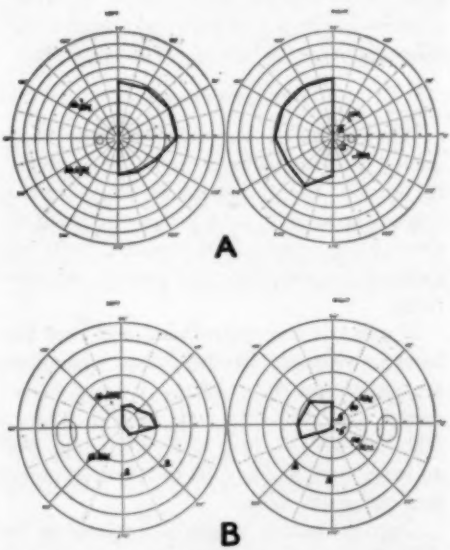


Fig. 2 (Chamlin and Davidoff). A. S. Case of pituitary tumor being treated with radiotherapy. Vision: O.D., 20/30—1; O.S., 20/200. (A) 2/330 white. (B) 1/2,000 white.

can see the 2-mm. white test object at five degrees in the 45-degree meridian and at 10 degrees in the 315-degree meridian. Such findings are seen in Figure 1.

Following the quality of defective field is especially important in observation of cases of chiasmal interference, particularly in those patients undergoing radiotherapy. The principles for such treatment were prescribed by Davidoff and Feiring,[3] and methods of examination were discussed in a previous paper.[4]

In such cases, the immediate effect of therapy may be that of edema around the chiasm, with encroachment on the field, especially the intermediate field. Critical, qualitative testing as already described will easily show such effect and enable the ophthalmologist to warn the radiotherapist to curb or modify the dosage.

More important, it will enable the ophthalmologist to give the neurosurgeon reliable warning of further or lesser encroachment on the chiasmal pathways without waiting for actual involvement of central visual acuity (Snellen). In this way, surgery can be performed earlier and more advantageously.

At this point we would like to discuss the subject of large test objects, or, greater stimulation in general. After finding that a patient cannot visualize 100-mm. white at 330 mm., we usually use hand movements. However, before using hand movements we will sometimes interject fingers between these two stimuli and indicate not only the ability to see fingers but the ability to count fingers.

If hand movements are not visible, one may use a large flashlight with a lens of about 60 or 70 mm. in diameter in a darkened room. Actually, flashing a large light in a darkened room is still another method of increasing the visual stimulus.

That is to say, instead of merely increasing the size of the stimulus, under standard lighting conditions (seven foot-candles), one increases the intensity of the stimulus by using an illuminated test object against a dark background, thus giving an even greater

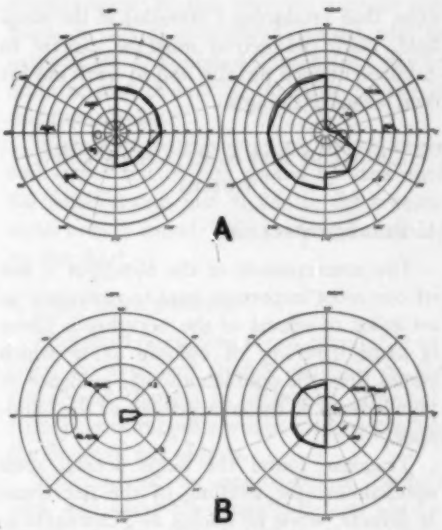


Fig. 3 (Chamlin and Davidoff). G. P. Case of pituitary tumor being treated with radiotherapy. Vision: O.D., 20/25—1; O.S., 2/200. (A) 2/330 white. (B) 1/2,000 white.

contrast than under standard conditions. It seems appropriate to label such testing as a change in the *intensity* of stimulus rather than in the *size* of stimulus.

A word of caution should be given regarding the use of such lights, and even the use of hand movements or other very large test objects.

Bright lights, as well as the reflected light from a large flat surface, such as a moving hand, or even the shadows cast by such a moving hand, may easily throw such a light or shadow on the side of the nose and it may be visualized by the patient in the seeing half of the field. The eager patient may report vision at this point, not realizing it is in the intact field. One must, therefore, be very careful about accepting the patient's word in cases such as these.

We have often found it useful to hold the straight edge of a large cardboard, such as the Jaeger charts for near testing, at right angles to the corneal surface, and very near it, so as to block any lights or shadows from the temporal field falling onto the side of the

nose, thus producing a stimulus in the nasal field. Each perimetrist must be careful to circumvent such pitfalls, and to work out his own means of doing so.

Choice of test objects for specific studies

1. Blindspot studies

The measurement of the blindspot is one of our most important tests in perimetry as an index of edema of the nervehead. There is some diversity of opinion as to which comes first, the ophthalmoscopic evidence of papilledema or the enlargement of the blindspot.

Traquair found the fields normal until ophthalmoscopic swelling of the nervehead is definite, while he quotes de Schweinitz as having found enlargement of the blindspot before ophthalmoscopic evidence of papilledema was present.

In our experience, we have found enlargement of the blindspot where ophthalmoscopic evidence of papilledema was still very scant, or at least the disc appearance was still compatible with normal. On the other hand, we have seen cases with definitely increased intracranial pressure and showing hyperemia of the discs but discrete margins and good physiologic cups, in which the blindspots fell within the one-degree pericecal zone of amblyopia.

In such cases, one cannot say whether or not the blindspot is enlarged unless he has knowledge of the previous measurements of this particular patient's blindspot. Since the exact mechanism of the production of papilledema is not definitely understood or agreed upon by all observers, one cannot give a definite explanation for the differences which have been mentioned.

It is our opinion that individual anatomic peculiarities may be important factors contributing to the presence or absence of papilledema in different patients with the same degree of increased intracranial pressure.

The anatomic features we refer to may be the size, depth, and shape of the physiologic cup and the physiologic status of the vessels —their permeability and points of entrance into and emergence from the optic nerve.

Other features that may influence the presence or absence of papilledema may be the size, number, and shape of the lamina cribrosa, the amount of perivascular striping on the disc, and the presence or absence of congenital membranes or glial tissue in the cup and the intraocular pressure.

A word must be said about the normal blindspot and the one-degree pericecal zone of amblyopia. The normal blindspot measures 5.5 degrees by 7.5 degrees, and is surrounded by a one-degree zone of diminished sensitivity where, in normal eyes, a 2/2,000 white test object may not be seen.

This brings the normal blindspot for 2/2,000 white up to as large as 7.5 degrees by 9.5 degrees. Thus, if a patient is suspected of early papilledema, a measurement of as high as 7.5 degrees by 9.5 degrees with 2/2,000 white may represent the normal blindspot for him, or a one-degree pericecal enlargement all around. Since one does not usually know the size of a patient's blindspot prior to such an examination, one may not be able to give a very helpful answer in such a case.

Enlargement beyond 7.5 degrees by 9.5 degrees with 2/2,000 white, in the absence of any visible peripapillary defects, such as a myopic or scleral crescent, medullated nerve fibers, or peripapillary choroidal sclerosis, must always be considered as strong evidence of true enlargement of the blindspot. Of course, any enlargement above 5.5 by 7.5 degrees which is also present for 5/2,000 white is even more significant of papillary edema.

When the enlargement can be shown with a 10/2,000 white or an even larger visual angle the ophthalmoscopic evidence is usually quite marked, and an enlarged blindspot is not necessary to make the diagnosis of papilledema.

It is apparent from these comments that minimal testing for enlargement of the blindspot should be carried out with 2/2,000 white. If this test shows the blindspot to lie within the 5.5 by 7.5 degree area, the blindspot may definitely be said to be within normal limits. We have never known a patient, in whom the disc measurements fell within these limits, who has shown any subsequent conclusive proof of having had papilledema at the time of the examination.

In short, measurements up to 7.5 by 9.5 degrees with 2/2,000 white may be within normal limits or may represent early enlargement, depending on the physiologic sensitivity of the peripapillary rods and cones, and can only be interpreted if a previous measurement of the patient's blindspot is available. Measurements beyond 7.5 by 9.5 degrees with 2/2,000 white, in the absence of any other visible peripapillary changes in the fundus should be considered as pathologic enlargement until proved otherwise.

2. Retinitis pigmentosa studies

Although the history and the fundus appearance are usually sufficient to make the diagnosis in pigmentary degeneration of the retina, peripheral field studies may be used to help diagnose or follow the course of such disease.

In early stages, an annular scotoma may be found even before the pigment is visualized. In advanced cases, of course, the defect may be dense even for hand movements. However, if the field is normal for 3/330 and 2/330 white, the periphery should be explored with 1/330 white in order to show early involvement, since the annular scotoma usually starts well in from the periphery and the 1/330 white isopter is closer to the vulnerable field in this disease.

Care must be taken to carry the test object all the way to fixation in each meridian, even after its initial recognition peripherally. The patient must continue to observe the test object all the way and indicate its disappearance at any point, as well as its subsequent reappearance. In this way, an annular scotoma, or part of an annular scotoma, may be mapped out. Diminished illumination may be quite helpful in picking up early defects in this type of case.

When scotomatous areas are found, larger and larger test objects should be used until the smallest one just visible in the scotomatous area is found. This should be recorded on the chart.

3. Glaucoma studies

This short discussion is not intended to replace the abundant studies available on the visual-field changes in glaucoma. However, some pertinent points will be made regarding the choice of test objects.

Widening of the angioscotoma, Seidel's sign, and nerve-fiber bundle defects are believed to show the earliest peripapillary changes, while peripheral depression may occur concurrently.

For the peripheral depression, again, 3/330 or 2/330 white may be used. If good expanse of field is still present for 2/330 white, then 1/330 white may be used. Diminished illumination, that is, using less than the standard seven foot-candles of light, will intensify such peripheral defects.

In testing the peripapillary area for nerve-fiber bundle defects, one must be sure to use a test object large enough to be seen normally within the pericecal area. Thus, a 1/2,000 white is a poor test for early nerve-fiber bundle defects near the disc since the 1/2,000 white, in most cases, does not reach out beyond the temporal border of the blindspot. A 2/2,000 white test is much more suitable for such early changes.

On the other hand, if searching for the end of a nerve-fiber bundle defect on the horizontal raphe *within the 10-degree arc*, the 1/2,000 white should be used because, in almost all normal cases, the 1/2,000 white field extends out to at least 10 degrees all around. Again, once a defective area is found, the quality of the defective area should be determined with larger stimuli.

4. Detachment of the retina and intraocular tumors

When a retinal detachment or tumor in the periphery of the retina is suspected, but not found ophthalmoscopically, one may employ peripheral visual-field studies to help discover them.

For such purposes, a 2/330 or even 3/330 white should be used. In any event, a test object large enough to extend to some portions of the periphery of the normal field must be employed so as to make sure that no portion of the peripheral field is excluded from the examination.

When a tumor or retinal detachment is suspected in the extreme periphery but cannot be visualized because of the very peripheral position, a defect in the peripheral visual field may be most helpful in diagnosing or locating the site of such lesions. In very mild detachments, however, very little perimetric defect may be demonstrable despite funduscopically visible detachment.

5. Macular degeneration

It is rare that macular degeneration requires visual-field studies for diagnosis. Usually the subjective complaints of diminution of central visual acuity and the appearance of the disturbed architecture in the macular area are enough to make the diagnosis. Visual angles as small as 0.5/2,000 white may have to be employed to demonstrate such lesions in the early stages.

Often we have found it rather difficult to demonstrate a field defect even in the face of definite ophthalmoscopically visible changes. We could not verify the usefulness of yellow and blue test objects to differentiate lesions involving the percipient elements rather than the nerve fibers.

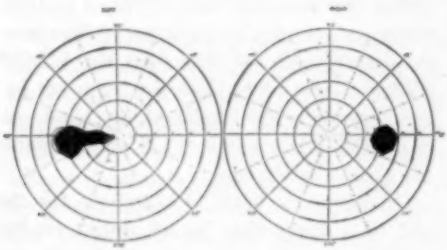


Fig. 4 (Chamlin and Davidoff). B. F. Case of retrobulbar neuritis in 31-year-old white woman, with a history of sudden blurring in left eye. Vision: O.U., 20/25. Blindspots, plotted with 2/2,000 white, showed a cecocentral scotoma, O.S., not quite reaching fixation. Clearing occurred in three weeks and was followed by nystagmus. A clinical diagnosis of multiple sclerosis was made.

6. Papilledema, optic neuritis, and retrobulbar neuritis

As already stated, for early papilledema the 2/2,000 white is the minimal test object of choice. Of course, the greater the visual angle with which the blindspot is shown to be enlarged, the more definite is the defect.

When not too dense, the cecocentral and central defects of optic neuritis and retrobulbar neuritis can often be shown with 2/2,000 white or 1/2,000 white. The dense nuclei within cecocentral scotomas are often brought out more dramatically with 5/2,000 red.

One should, however, use the *largest test object possible* that still brings out the defect. Then, if a smaller test object is definitely visualized within this area on a subsequent visit, we have good proof of improvement. Such proof of improvement may be a great help in labelling the defect as due to an inflammatory lesion rather than to an intracranial mass lesion, and thus avoid needless air studies or angiography.

A word of caution is in order regarding a patient's complaint of sudden onset of blurred vision, although, when tested on the Snellen chart, he still reads 20/20 or even 20/15. One must remember that the presence of good visual acuity (Snellen) does not preclude a diagnosis of optic or retrobulbar neuritis. In such cases, great care must be taken to search for nerve-fiber bundle defects, skirting around, but not quite involving fixation. Also, pericentral scotomas not quite reaching fixation may be present, such as in Figure 4.

In cases in which papilledema has been known to exist for some period of time, a certain amount of peripheral contraction usually has taken place. In such cases, the periphery must be tested with 2/330 or even 3/330 white.

If both of these show normal contour to the field, but the extreme periphery of the physiologic field has not been reached, then a 5/330 white should be used. When the findings for 5/330 white do not reach to the physiologic periphery, then one may logically assume that this case has a certain amount of peripheral depression which may well be the result of prolonged papilledema.

7. Congenital and developmental anomalies of the optic disc

Under this heading we will consider pseudopapilledema and congenital hyaline tissue of the optic nervehead. The term pseudopapilledema is applied to a rather vague group of cases in which the discs show blurred margins, thus giving the appearance of early edema, but in which the blindspot is normal in size. In such cases, a blindspot that is no larger than 7.5 by 9.5 degrees with a 2/2,000 white may be considered as good functional proof of the absence of papilledema.

Drusen and amorphous hyaline tissue of the disc may occur as a congenital or developmental anomaly and cause enlargement of the blindspots, as shown in our recent report dealing with this subject.[6] While the enlarged blindspot due to papilledema is apt to show progressive enlargement over a period of days or weeks, that due to hyaline tissue remains relatively fixed for years at a time or does not change at all.

Again, enlargement beyond 7.5 by 9.5 degrees with 2/2,000 white may be used as proof of enlargement. In both papilledema and hyaline tissue of the disc, when the enlargement exists for a larger visual angle, such as 5/2,000 white, then it is even more definite that these blindspots are enlarged.

8. Optic atrophy

While various criteria have been offered to differentiate atrophy from physiologic pallor, we have found, in questionable cases, that the only reliable criterion is that of a functional test—that is, the field of vision. For such purposes, the entire field must be tested—peripheral, intermediate, and central—as well as the blindspot.

Defects will depend on the initial lesion having caused the atrophy. Thus, if the atrophy is due to prolonged increased intracranial pressure, one may find a mild peripheral depression for 2/330 or 1/330 white. If the optic atrophy is due to former retrobulbar neuritis which had shown a cecocentral scotoma, then one may have to use minimal test objects such as 1/2,000 white, or, more centrally, 0.5/2,000 white or 3/2,000 red, to bring out the remains of such earlier defects. In any event, the field must not be considered as normal until every portion of it has been explored within minimal test objects.

9. Intracranial interferences with the visual pathways

Interference with the optic nerves just inside the cranial cavity is usually characterized by a peripheral depression which may extend centrally to involve fixation. Some observers have described the central defect as appearing quite early and as being more dense than the peripheral one. When reporting central defects, one must try to qualify the defect by finding how small a stimulus can just be made out in this scotoma.

Peripheral defects due to mass pressure are usually easily demonstrated with 1/330 white. On the other hand, in very early mass pressure on an optic nerve, only the extreme periphery may be involved, thus requiring exploration of the 5/330 isopter to demonstrate such defect.

In such a case, the inner peripheral isopter, such as 1/330 or 1/250 white, may not yet show any involvement. For an example, see

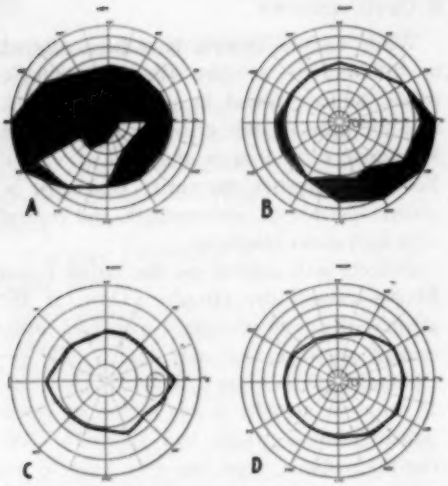


Fig. 5 (Chamlin and Davidoff). D. W. Osteofibroma arising from left olfactory groove in a 25-year-old white woman. Vision: O.D., 15/15; O.S., Counts fingers. (A) Left field for 10/250 white. (B) Right field for 5/330 white, showing beginning contraction in extreme periphery. (C) Right field for 1/250 white. This inner isopter of the periphery does not yet show any contraction. (D) Right field for 1/2,000 white. This more central isopter also shows no contractions.

Figure 5. Subfrontal and sphenoid-ridge meningiomas have been found to cause such peripheral depressions in the early stages.

In the chiasmal area, mass interference begins to show hemianopic features. The field affected earliest lies between 10-25 degrees, or the so-called "intermediate field," and minimal testing for defects here is best done with 1/2,000 white.[4]

Peripheral fields for 1/330 white should be done as well, although, as a rule, the 1/2,000 white shows the earliest and greatest amount of involvement in chiasmal interference (fig. 1).

Here again, when temporal defect is present for 1/2,000 white, the defective area around 10 degrees or so should be explored with larger and larger stimuli, until the density of this defect is ascertained and noted. Such careful plotting would explain otherwise obscure subjective complaints.

For example, on one occasion, the patient whose field is represented in Figure 6 came in complaining of loss of vision in the right eye. On examination, her fields for 2/330 white, 1/2,000 white, and visual acuity were unchanged. However, although she had previously seen hand movements at 2,000 mm. on the 11-degree arc in the 45-degree meridian, she now could no longer do this, as shown in Figure 6-B. Since this was her better eye and she leaned heavily on it for her purposes, she became aware of this loss. Radiation therapy was started again with improvement in the recently affected area.

Certainly, in such a case, mere routine testing of visual acuity, and 2/330 as well as 1/2,000 white, would have shown no change from the previous examination, and the patient would have been accused of being neurotic, when she really needed help. Mass lesions most commonly encountered in this area are suprasellar meningiomas, pituitary tumors, craniopharyngiomas, and aneurysms.

Tract interference is characterized by in-

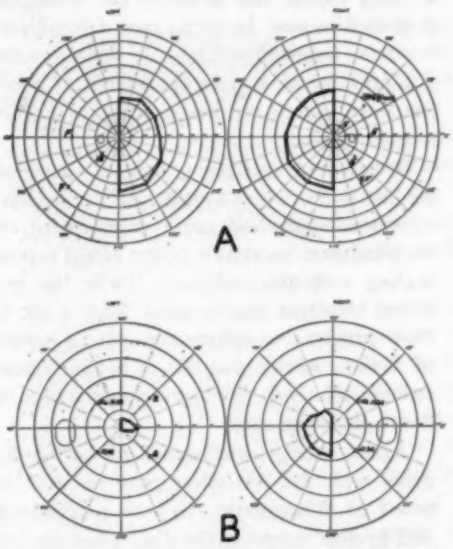


Fig. 6 (Chamlin and Davidoff). R. R. Case of pituitary tumor being treated with radiotherapy. Vision: O.D., 20/40; O.S., 20/200. (A) 2/330 white. (B) 1/2,000 white.

congruous homonymous hemianopic defects. Usually, tests with 2/330 or 1/330 white show these up best, while 1/2,000 white usually brings out the same defect or even more of it. As before, larger and larger test objects should be used in the defective field, until the smallest one just seen is found and indicated on the chart. The most common cause of tract interference is probably tumor.

Above the geniculate bodies, interference causes homonymous hemianopia, more congruous and with more chance of macular sparing. As the fibers spread out from the geniculate bodies, small groups of fibers may be involved independently of others so that the ventral radiations of Meyer's loop may be involved in temporal lobe tumors to give an upper homonymous hemianopia without involvement of the lower half of the field.

Again, 1/330 and 2/330 white is best suited for demonstrating such defects, and too much stress cannot be laid on the need for minimal testing with these stimuli, especially when searching for minimal hemianopic defect as explained in a previous study.[3] Furthermore, the defective areas must again be qualified by the smallest stimulus just visible there.

Evaluating the quality of defective field may prove very helpful in diagnosing or following such cases clinically. For example, Figure 7 shows the case of a young man who developed a left homonymous hemianopia, dense even to hand movements. Complete neurologic examination, including electroencephalography and pneumo-encephalography revealed no definite evidence of an intracranial mass. The patient was discharged from the hospital, to be followed in the office.

There was gradual improvement of the defective area, so that, five months later, the upper left field returned for 5/250 white, and the lower left field for hand movements. Four months later, the upper left field returned for 3/250 white, although the lower left homonymous field did not improve further.

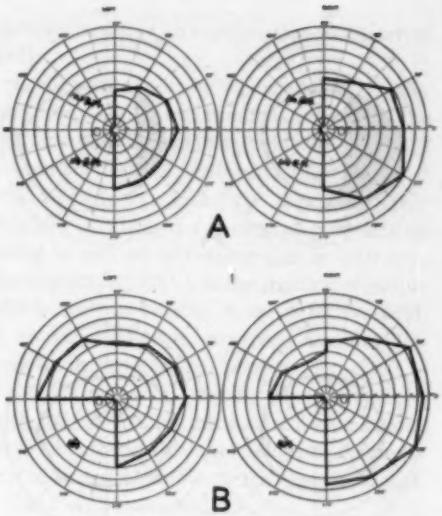
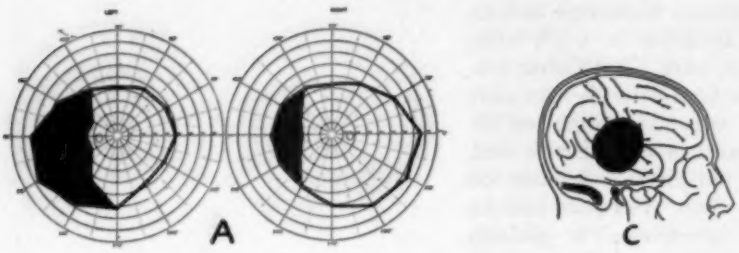


Fig. 7 (Chamlin and Davidoff). B. P. Case of sudden onset of homonymous hemianopia in young man. Neurologic examination otherwise completely normal. Slow but definite improvement in quality of the left homonymous field over several months. (A) June, 1949: 1/250 white. (B) November, 1949: 5/250 white. In November, 1949, the right homonymous field remained full for 1/250 white, and the 5/250 white field was plotted.

At this time he had no subjective complaints. Visual acuity remained 20/15 in each eye throughout the entire period. If only a 2/250 field were done, and the defective area not qualified further, the examiner would not be aware of the improvement. If only hand movements were used, recovery would have been considered complete five months after the onset of the illness. Later on, the upper left homonymous field returned for 1/250 white, but the lower homonymous field showed no further improvement.

The persistence of greatest loss of vision in the left lower homonymous field may be taken as evidence of earliest and most severe interference in the dorsal portion of the involved level of pathway. This was in agreement with the patient's history that the initial loss was in the lower left field, followed by that in the upper.



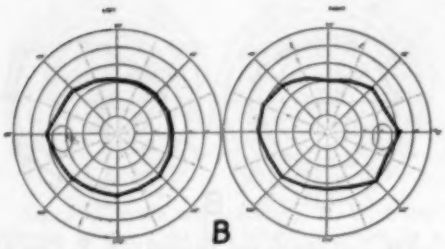


Fig. 8 (Chamlin and Davidoff). Elderly white woman with pneumo-encephalographic evidence of a mass in the right temporoparietal area. Craniotomy revealed temporoparietal meningioma, 5.0 cm. in diameter. Vision: O.D., 20/200 (old amblyopia ex anopsia but the central defect was not plotted); O.S., 20/20. (A) 2/250 white. (B) 1/2,000 white. (C) Postoperative sketch showing site of tumor.

A diagnosis of some accident due to a vascular malformation or possibly multiple sclerosis was considered.

Using the various test objects showed a definite, progressive improvement. While a definite diagnosis has not been made, at least one can feel reasonably certain that the pathologic process is receding—fairly good evidence against an expanding intracranial lesion.

More posteriorly, as one approaches the occipital lobe, tumors and vascular lesions may cause homonymous hemianopia, the peripheral field showing the greatest involvement, with the 1/2,000 white usually showing corresponding involvement.

We have found 10 cases showing incomplete homonymous hemianopic defect in the periphery for 1/330 or 2/330 white, but with much less, or even no, involvement of the intermediate field for 1/2,000 white. In two cases, a brain tumor was demonstrated surgically. One of these cases is illustrated in Figure 8.

Finally, in the posterior part of the radiations, that is, in the occipital lobes, lesions

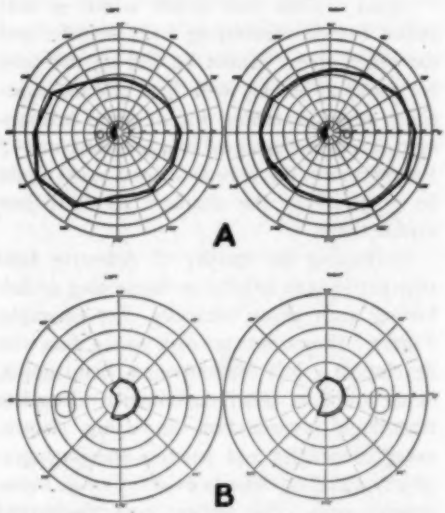


Fig. 9 (Chamlin and Davidoff). J. R., 31-year-old white woman with two-month history of transient episodes of blurring on left side. These episodes became more frequent and the blur finally remained permanent. Complete neurologic investigation including pneumo-encephalography and angiography failed to establish a diagnosis. Closure of a small vessel in the tip of the occipital lobe was considered the most likely diagnosis. Vision: O.U., 15/15. (A) 2/330 white. (B) 0.5/2,000 white. The scotomatous area was dense even to 10/2,000 white.

will produce paracentral homonymous defects without involving the periphery of the field (fig. 9). In such cases, the periphery remains completely normal for minimal test objects, while the homonymous paracentral defect, which may or may not reach the midline, may be quite dense.

In the case illustrated in Figure 9, the periphery was normal for 2/330 white, while the paracentral defect was dense, being absolute even for 10/2,000 white.

Similar defects have been described by Gordon Holmes in injuries to the tip of the occipital lobe.[7]

Summary

1. Peripheral, intermediate, and central fields, as well as blindspots, may be involved independently or in combination in defective fields.

2. Before reporting visual fields as normal, one should use minimal testing in the various portions of the field. Criteria are presented for such minimal testing.

3. In defective areas, the depth of defect should be indicated for clinical purposes by using stimuli of increasing size or intensity, thus indicating which is the smallest stimulus which can just be seen in the defective field. A simple method is presented for showing such findings on the field charts.

4. The common causes of interference with the ocular and intracranial visual pathways together with the field involvements and choice of testing materials are discussed.

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BUPHTHALMOS

Results from operative procedures particularly cyclodiathermy: Report of six cases

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The treatment of buphthalmos or juvenile glaucoma has progressed markedly in the last quarter of a century. The literature contains a number of reports of successful surgical procedures used in treating this abnormality.

Holmes[1] reported a case in which the patient suffered an injury, in 1936, to an eye operated on in 1911 by Dr. Ben Witt Key of New York. In the interim, sufficient vision had been regained for the patient to finish grade school. A case in which the patient was kept under observation for 17 years was reported by Spratt.[2] In two cases reported by Mengel,[3] infantile glaucoma was controlled in three eyes by trephination.

Associated with the trephining operation, such operative complications as loss of vitreous and subsequent phthisis bulbi have frequently been reported. It is generally agreed that the surgery of buphthalmos is much

more difficult than the average glaucoma surgery. Barkan[4] contributed notably to the technique of goniotomy.

My purpose in this paper is to present my conclusions that some early and late cases of buphthalmos respond to some of the older procedures, especially to cyclodiathermy used conservatively. In five cases here reported intraocular surgery produced little improvement in the intraocular pressure, but cyclodiathermy effected its control. In Case 1, cyclodialysis was followed by cyclodiathermy in 1943 when the patient was only a few weeks old; the child is now in school and able to carry on well.

Satisfactory results in Case 4 were obtained by an iris-inclusion operation combined with corneosclerectomy, a modified Lagrange operation; even the cloudiness completely disappeared in the cornea of one eye.

Report of cases

Case 1

R. D. F., aged three weeks, a first child normally delivered, was examined in March, 1943, because the mother thought the infant was blind. The family history was noncontributory.

On *ocular examination*, there were noted blepharospasm, searching nystagmus, faint ciliary blush of the globes, very thin sclera, edema of the corneas manifested by cloudiness and a thin bluish haze centrally, deep anterior chambers, blurred iris structure of homogenous appearance with many details missing, and small pupils reacting sluggishly. The corneas measured 14 mm. both horizontally and vertically. No view of the eyegrounds was obtainable. Intraocular pressure ranged from 75 to 89 mm. Hg (Schiøtz) on several examinations in spite of the use of pilocarpine and eserine.

On April 5, 1943, bilateral cyclodialysis in the upper temporal quadrant, involving separation with the spatula of at least one third of the corneal circumference, was performed. There was little postoperative reaction, and massage and miotics were started early. The intraocular pressure, however, was 75 mm. Hg a week later. Bilateral cyclodiathermy, consisting only of a surface nonperforating diathermic procedure, was carried out on April 15th in the lower nasal quadrant, extending up into the upper nasal quadrant.

Eight days later the intraocular pressure was 35 mm. Hg in both eyes and it did not exceed 41 mm. Hg until July, when it was 56 mm. Hg in the right eye and so high in the left eye that it did not register on the scale. On July 12th, cyclodiathermy was again performed on the temporal halves of the eyes. The intraocular pressure on August 24th was 35 mm. Hg in both eyes; on September 30, 1943, and January 2, 1944, it was 30 mm. Hg. The corneal haze had completed disappeared.

Four and a half years elapsed before the child was heard from again. On May 31, 1948, he was brought in for refraction prior to entering school, his parents suspecting defective vision in the right eye. There was slight nystagmus in both lateral positions. The corneas measured 14 mm., horizontally and vertically, and the areas where the cyclodiathermy had been performed showed clearly. No corneal opacities were observed, but biomicroscopy revealed some linear defects centrally, undoubtedly in Descemet's membrane. The anterior chambers were normal in depth. The pupils were extremely small and somewhat irregular; they reacted hardly at all to light or accommodation.

The irises presented an unusual blurring of details, a flat surface, and alteration of the pigment of the collarette. The picture was not, however, one of atrophy. In the right eye there was slight iridodialysis where the cyclodialysis had been performed.

Gonioscopic examination revealed much mesenchymal tissue in the angle of the anterior chamber and the suggestion of a cleft in both eyes where the cyclodialysis had been performed. No view of the eyegrounds was obtainable because of the small pupils. Skiascopic examination was not possible as no red reflex could be made out.

Vision in the right eye was 20/200 and in the left eye, 20/60, correcting with a —4.0D. sph. to 20/50 in the right eye and with a —1.5D. sph. to 20/40 in the left eye. All tests were repeated several times, Regan's preschool chart being used. At near, J4 was obtained in the right eye and a J1 in the left eye.

Examination of the visual fields was attempted, but was not satisfactory. The intraocular pressure was 18 mm. Hg (Schiøtz) in the right eye and 22 mm. Hg in the left eye.

After atropine and paredrine had been used in each eye for 24 hours, the pupils had dilated to between two and three mm. Skiascopic examination showed for the right eye: —3.0D. sph. ⊂ —1.0D. cyl. ax. 45°, and for the left eye, —0.5D. sph. ⊂ —1.0D. cyl. ax. 97.5°. Under a cycloplegic, the corrected vision was 20/50 in the right eye and 20/30 in the left eye. Pronounced cupping of the disc and displacement of the vessel funnel to the nasal side were present in the right eye but not in the left.

Intraocular pressure was 38 mm. Hg in both eyes under the effect of the cycloplegic. Philocarpine was administered and was prescribed for home use for a few days. Two days after the use of the cycloplegic, the intraocular pressure was 22 mm. Hg and 30 mm. Hg in the right and left eye, respectively; three days later it was 18 and 22 mm. Hg. On two subsequent monthly examinations, without the use of a miotic, the pressure was 18 mm. Hg in the right eye and 22 mm. Hg in the left eye.

When the patient was last examined on September 1, 1950, the corrected vision was 20/100 in the right eye and 20/30 in the left eye. In both eyes, the intraocular pressure was 28 mm. Hg and the corneas were perfectly clear. He attends the regular classes in the public school and does well.

CASE 2

N. C., a girl, aged three months, an only child delivered normally, was examined on March 1, 1935. The mother had noticed immediately after the child was born that the corneas were bluish gray and the eyes were large. Apparently vision was better in the left eye. The family history was irrelevant.

On *ocular examination*, the globes were prominent, the conjunctiva was normal in appearance, and searching nystagmus was present. The sclera seemed extremely thin. The corneas measured 13.5 mm. horizontally; in both, there was a complete bluish gray haze of a uniform type. No view of the anterior chamber could be obtained. The intraocular pressure was 80 and 75 mm. Hg (Schiøtz) in the right and left eye, respectively. In all, the picture was typical of buphthalmos.

General examination showed a peculiarly shaped head suggestive of hydrocephalus. The fontanels were extremely large.

Dr. J. J. Regan of Boston saw the baby with me, and on the following day he performed a bilateral iridotasis. The intraocular pressure was controlled for about 10 days. This operative procedure was followed in the next three months by a bilateral paracentesis and three different cyclodialysis operations with the result that the pressure was finally controlled until early in 1936.

In 1942, six years later, the child returned for tonsillectomy. The intraocular pressure, taken while the patient was under the anesthesia, was 50 mm. Hg in each eye. The ocular examination gave about the same results as six years previously. There was, however, much less corneal haze in the left eye than in the right.

Dr. Regan saw the patient again that year and changed the ocular therapy from mecholyl and prostigmine to neosynephrine emulsion. Multiple vitamin therapy was also prescribed. No other surgery was advised.

After a lapse of another six years, the child was again seen in early August, 1948. There had developed a deafness so severe that the use of a hearing aid was required. The mental condition was much retarded. The voice was most unusual, but understandable. Locomotion was somewhat difficult.

On *ocular examination*, the right globe appeared to be a little smaller than the left. The cornea of the right eye was very opaque with a band-shaped calcareous degeneration. There was much less corneal haze in the left eye, although no details of the anterior chamber could be made out. The mother stated that the child was blind in the right eye, but could get around in familiar places with the vision present in the left eye.

Fig. 1 (Forbes). *Case 2.* This photograph of the round penetrating six-mm. corneal transplant was taken 17 months postoperatively. No iris is visible since the peripheral cornea is completely opaque.

Functional examination indicated bare light perception at four feet in the right eye. There were, however, good light perception and projection at 20 feet in the left eye. Color perception was good, as was macular perception. Also, hand motion perception was present in this eye. The intraocular pressure was 85 mm. Hg in the right eye and 61 mm. Hg in the left eye.

Bilateral perforating cyclodiathermy, following the technique of Stocker,[8] was performed. One half the circumlimbal circumference was covered with the punctures. One month later, the intraocular pressure was elevated in the right eye but lower in the left eye. Seven months postoperatively it was 40 mm. Hg in the right eye and 30 mm. Hg in the left eye. There was light perception at 10 feet in the right eye, and hand motion perception was better in the left eye.

The patient was seen twice in 1949 with normal intraocular pressure in the left eye, 22 mm. Hg in February and 26 mm. Hg in August. The right eye had a normalized intraocular pressure but little light perception. Under pentothal sodium anesthesia, a round penetrating six-mm. corneal transplant was done on the left eye on September 1st.

In the 17 months that have elapsed since that time the intraocular pressure in this eye has not been above 34 mm. Hg, and the transplant has remained clear, as shown by a photograph taken in January, 1951 (fig. 1).

Beta irradiation has been used for the prevention of vascularization and subsequent clouding of the transplant. Pilocarpine is being used in the eye three times daily. Gross form perception is present, and finger perception is present at 10 feet.

CASE 3

H. T. A., Jr., aged five years, was examined on October 31, 1947. He had never walked or talked.

Congenital cataracts were present. In 1944, the right eye had been needled once and the left eye twice. The vision had been growing worse, but the patient would not wear an aphakic lens.

On *ocular examination*, a searching nystagmus was noted, also a very thin sclera, a central bluish haze of the corneas, deep chambers, sluggish pupillary reactions, and fairly clear pupillary areas. The eyes were aphakic. The structure of the iris presented a rather homogenous appearance. It was difficult to obtain a view of the eyegrounds. The intraocular pressure was so high that it was impossible to register it with a standard Schiøtz tonometer.

The corneal measurements were 13 mm. in each eye at the time surgery was undertaken. Cyclodialysis with separation of about one third of the limbal circumference with the spatula was performed. Postoperatively, the reaction was slight. Considerable hypotony resulted in the right eye; the intraocular pressure in the left eye was 12 mm. Hg.

For two months the intraocular pressure was normalized, but at the end of the third month both globes were so hard that the pressure barely registered. At this time perforating cyclodiathermy was performed in the upper temporal quadrant bilaterally. Four months later cyclodiathermy was repeated, this time in the lower nasal quadrants. The intraocular pressure has since remained under control in the right eye. Six months postoperatively, it was 26 mm. Hg in the right eye; in the left eye it was 48 mm. Hg. Another conservative cyclodiathermy on the left eye is contemplated.

Present treatment consists of carcholin, pilocarpine, and eserine in one prescription and also neosynephrine emulsion twice daily in the right eye and four times daily in the left eye. The corneas have cleared almost completely, and a view of the eyegrounds can now be obtained. There is decided cupping of the discs and displacement of the vessel funnels.

The parents insist that the child sees better. In view of the pronounced microcephalia, total absence of speech, and loss of motor control of the lower extremities, he could probably be classified as an imbecile.

CASE 4

R. C., aged six years, and an only child, was referred by Dr. Sherrel D. Patton of Sarasota on December 7, 1948. The complaints were severe frontal headaches apparently of ocular origin and a bloody discharge from both nostrils. Oculists had stated that glaucoma was present in both eyes. The left eye had become much worse recently with a white cloud appearing over the center. The family history was indefinite; the mother had died early. There was apparently no injury at birth, but there had been some plastic work done for talipes.

Ocular examination. Moderate injection of both globes was noted on ocular examination, also advanced limbus and rather pronounced focusing nystagmus. In both eyes, the cornea measured 14 mm.

In the right eye the chamber was especially deep, and there was questionable iridodonesis. In the iris of this eye, a considerable amount of mesenchymal tissue was present in the angle. Gonioscopy was carried out on this eye without much difficulty. There were many anterior trabeculas extending over to the angle. The pupil, slightly oval in shape, reacted sluggishly. In the fundus there were cupping of the disc, displacement of the vessel funnel to the nasal side, and a perineural halo.

In the left eye, a diffuse corneal haze, typical of buphthalmos, was present. No view of the anterior chamber could be obtained.

Intraocular pressure in both eyes varied from 40 to 50 mm. Hg (Schiøtz) at various examinations despite the miotic prescribed by Dr. Patton prior to transferring the patient to my care.

Reaction to the intradermal Mantoux test gave negative results locally, focally, and generally. The child was referred to a pediatrician who advised waiting for improvement in his general condition before subjecting him to surgery.

In early December, 1948, iridencleisis combined with corneosclerectomy, a modified Lagrange operation, was performed on the left eye. A month later, with a 10-mg. weight, intraocular pressure registered 26 mm. Hg in the left eye, but the right eye was so hard that the pressure did not register on the tonometer. The same operative procedures were then carried out on the right eye.

The cornea in the left eye began to clear rapidly, and in three weeks after the operation on the right eye, the intraocular pressure did not register, the eye was so soft. At this time, two months after the operation on the left eye, the intraocular pressure in this eye was 13 mm. Hg.

Two months after the operation on the right eye and three months after the operation on the left eye, the intraocular pressure was extremely low in both eyes. Seven months after the operation on the right eye and eight months after the operation on the left eye, it was 12 mm. Hg in the right eye and 14 mm. Hg in the left eye. The vision was 20/200 in each eye.

The cornea had cleared in the left eye sufficiently to permit a good view of the fundus; cupping of the disc, displacement of the vessel funnel, and perineural halo could be seen.

Boiled milk injections were advised over a considerable period of time. Throughout the whole course vitamin B_1 and a mixed vitamin were prescribed along with a choline chloride drop for use in the left eye. Biomicroscopic examination of the left eye revealed defects around Descemet's membrane and some stromal mottling. Gonioscopic examination disclosed blockage of the angle with bands of tissue extending across the angle.

On September 9, 1950, ocular examination was again made. Both eyes were white and quiet. Motility was fairly good. The corneal measurements

were 13 mm. in each eye. There was a nice filtering bleb above in both eyes with an iris coloboma due to an iris inclusion operation.

The cornea of the left eye showed a few vessels coming down from above, deep vessels and some moderate, deep corneal scarring defects, apparently in Descemet's membrane and the deep stroma. The eyegrounds showed definite cupping and displacement of the vessel funnels in both discs. The media other than the corneas were fairly clear.

Intraocular pressure was 30 mm. Hg in the right eye and 16 mm. Hg in the left eye. On ophthalmoscopic examination the right eye was viewed with a rather high minus lens in the ophthalmoscope and the left eye with a rather high plus lens; therefore, a glass prescription was given on that basis.

The visual fields were questionable. The central fields, including the blindspots, were not obtained. Gonioscopy showed embryonal tissue in the angle and anterior trabeculas. The vision was 20/100 in the right eye and 20/200 in the left eye.

CASE 5

K. H., aged three years, an only child born normally, had apparently not been able to see since birth. Several operations on both eyes appeared to have given no relief.

Ocular examination on February 2, 1949, when I was first consulted, revealed great injection of the globes, intense corneal edema in both eyes with the cornea of the left eye below being markedly hazy, and deep anterior chambers. There was an iridotomy of a trephination above in the right eye with apparently no filtration and two in the left eye, one at the 12-o'clock meridian and one to the temporal side. There was filtration in the bleb at the site of the temporal trephination in the left eye. Some vascularization of the iris was present. A good view of the fundus could not be obtained.

In both eyes the corneal dimensions were 15 mm. in the vertical and horizontal meridians. The eyes were so hard that the intraocular pressure did not register on a Schiøtz tonometer with a 10-mg. weight. The patient was referred to a pediatrician, who pronounced the condition satisfactory for further operative work.

On February 11th, penetrating cyclodiathermy was carried out on the lower half of the globe in both eyes from the mesial to the lateral rectus. At the same time, cyclodialysis was performed above from the upper temporal side with a rather wide sweep of the spatula in the chamber and back into the suprachoroidal space.

The intraocular pressure did not stay down long, running between 54 and 49 mm. Hg in the right eye three weeks after the operation and up to the midforties in each eye five weeks postoperatively. Six weeks after the original operation, another cyclodiathermy of the same type was performed on the upper third of the globe. Intraocular pressure was at high normal 11 days after the operation. Thereafter, hypotony developed in both eyes and lasted for several weeks, with the intraocular pressure gradually returning to normal.

In late October, seven months after the last operation, the intraocular pressure was 30 mm. Hg in each eye without medication. There was improvement in the corneal condition, but a view of the fundus could not be obtained. Seclusion of the pupils and some secondary lens changes were noted. There apparently was some improvement in the visual function, but how much was difficult to ascertain. The intraocular pressure, however, was within the upper limits of normal, and apparently no damage resulted from the hypotony of several weeks' duration.

Examination on September 1, 1950, revealed that both corneas had cleared fairly well. The intraocular pressure was 26 mm. Hg in each eye. Light perception and projection in both eyes were good. There were lenticular opacities in both eyes, and I plan to go ahead with operative procedures, discissions, for the secondary cataracts.

CASE 6

H. M., aged five years, was examined on May 3, 1949. When the child was three months old, the parents had noticed that both eyes looked cloudy and that the vision seemed poor. He could now, however, see objects at a distance in the light and colors at near. The delivery had been normal. There was one brother, aged two years, with no ocular disturbance.

The ocular findings were typically buphthalmic with diffuse corneal clouding in both eyes, more pronounced in the left eye. The horizontal corneal dimensions were 15 mm. in the right eye and 17 mm. in the left eye. The chambers were deep. There was great sensitivity to light with any bright light causing an attack of sneezing, intense corneal edema, considerable vascularization of the cornea, and central opacity in the left eye. No view of the grounds could be obtained.

Light perception and projection were good at 10 feet in both eyes. Color perception was good at near. Intraocular pressure was so high that it could not be registered by a Schiøtz tonometer with a 10-mg. weight. A pediatric survey indicated that the general condition of the patient was satisfactory for surgery.

At operation, 12 days after the first examination, bilateral perforating cyclodiathermy was carried out, including the lower half of the circumcorneal area from the mesial to the lateral rectus, and cyclodialysis was performed on the upper temporal quadrant.

The intraocular pressure was 38 and 45 mm. Hg in the right and left eye, respectively, 17 days after the operation, and about the same a week later. Two months postoperatively, it was so low in the right eye that it did not register; in the left eye it was at the upper limit of normal, 30 mm. Hg.

The hypotony persisted in the right eye for about

Fig. 2 (Forbes). *Case 6.* Taken two months postoperatively, this photograph shows the result of penetrating keratoplasty on the left eye.

three weeks; three months after the operation, the intraocular pressure was within the upper limits of normal. Hypotony occurred in the left eye three months after the operation and remained present for a period of six weeks. The intraocular pressure five months after the operation was 30 mm. Hg in the right eye and 12 mm. Hg in the left eye, without medication. There was improvement in the corneal condition.

As there was considerable vascularization of the cornea, beta irradiation with a 20-mc. applicator was employed for the obliteration of the corneal vessels and for the improvement of the corneal scarring. The visual function was definitely improved, perception of gross hand motion being present at five feet in each eye.

Apparently the intraocular pressure is normalized for it was within normal limits on February 26, 1951. A penetrating keratoplasty later was performed on the left eye on May 9th with gratifying success (fig. 2).

Discussion

Cyclodiathermy was used in five of the six cases of this series. In three cases it followed cyclodialysis and in two was performed in conjunction with it. In Case 2, it followed unsuccessful intraocular operative procedures and, in Cases 1 and 5, it was repeated.

In nine of the 10 eyes the intraocular pressure was normalized. In one eye it was fairly normal with the use of miotics. In Case 1, in which cyclodiathermy followed cyclodialysis performed early, the visual function was retained to the extent that the child was able to go to school and the intraocular pressure was normal.

In Case 4, treatment consisted of an iris-inclusion operation in one eye and an iris-inclusion operation combined with a corneosclerectomy in the other eye. The corneal haze cleared sufficiently to give a clear view of the grounds, and there was great improvement.

These operations are, of course, old procedures. I am under the impression that goniotomy would be a most difficult procedure in the late type of buphthalmos with the highly opaque cornea. In these late cases, Schlemm's canal is usually closed; in all probability, therefore, an angle operation would not be of much value. It would seem that cyclodiathermy should have a place in the surgical armamentarium for this type of case. In none of the 10 eyes did global shrinkage develop, which has been feared in this type of surgery.

Summary

Six cases of buphthalmos are reported. They illustrate the therapeutic value of older surgical measures, particularly cyclodiathermy.

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A SCREW-TYPE IMPLANT

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Numerous types of implants for use following enucleation or evisceration have been described. Descriptions of the more popular ones, usually carrying the designer's name, may be found in papers by Mules,[1] Wheeler,[2] Ruedemann,[3] Cutler,[4] Berens,[5] Hughes,[6] Dimitry,[7] and Durham.[8] Dimitry[7] gave an excellent account of the history of enucleation and evisceration up to 1944.

Since all types have their advantages and their champions, it would appear desirable to decide on the criteria which should determine the choice of implant in any particular case.

CRITERIA FOR CHOICE OF IMPLANT

1. MOVEMENT

Motion of the prosthesis should be instantaneous in at least the four directions from the primary position possible in the vertical and horizontal planes. It is ideal if the rotation is equal to that of the sound eye, but this is not essential. It is more important that the prosthesis move at the same instant as the remaining eye.

Fairly large degrees of deviation of the visual axes in two otherwise normal-looking eyes will not be noticeable to the average observer if simultaneous movement from the primary position takes place. Since it is now possible to get a prosthesis which is almost identical with the remaining eye in color, size, and texture, it seems that any fault lies in the lack of instantaneous movement of the prosthesis with movement of the sound eye.

2. PERMANENCY OF THE IMPLANT

Even if ideal movement is realized, if a high percentage of the implants extrude, the end result is less desirable than if a simple glass sphere had been inserted. The possibility of extrusion has deterred many ophthalmic surgeons from using modern implants.

3. TECHNICAL DIFFICULTIES

Nearly all implants require particular care in the isolation of the recti muscles and their subsequent proper suturing. Likewise, care in the closure of Tenon's capsule and the conjunctiva is important. Some of the recently designed implants present special problems because of their relatively complicated nature. Many of the implants have provision for suturing live tissue to inert material. The proper amount of tension to place on the sutures may be a factor in influencing the permanency of the implant.

4. COST OF IMPLANT AND PROSTHESIS

The unit cost would probably not be important if there was adequate time for planning enucleations. Unfortunately, many eyes are removed in an emergency. Because of this, most ophthalmic surgeons prefer to have implants on hand.

Many of the implants require a specially fitted prosthesis. Many of the combinations come in different sizes. There are many different types to choose from. This has now become a confusing problem because of the increasing number of implants of various designs. I am certain that the overall cost and complexity of choice make surgeons fall back on the simple, yet inadequate, glass spheres.

5. SKILL IN FITTING THE PROSTHESIS

This technique is not in the domain of the surgeon but it is his responsibility to know a technician or artisan whom he can rely on for real skill in the fitting of the prosthesis. The problem of lid sag belongs almost exclusively to the technician who can design the prosthesis to meet this condition.

The simple glass ball or Wheeler grooved ball, both of which are popular, meet the criteria of permanency, are easy to insert,

and are reasonable in cost. There is usually a good stump and the technician has no difficulty in matching the eye. Unfortunately, movement is not instantaneous. Consequently, the artificial eye is more obvious and leaves much to be desired from the cosmetic standpoint.

The Cutler ring or "basket" implant has a high percentage of extrusions, is comparatively difficult to insert, and is expensive. One advantage of the "basket-type" implant, of which there are now several, is that it imparts the best motion of all types described to date.

Because of its size, the Ruedemann combined implant and prosthesis is useful in a very narrow field. Unfortunately, extrusions are common.

Other implants recently introduced[9-14] have the advantage of good movement, like the Cutler implant, but are not popular because they are unsatisfactory from other points of view.

Screw-type implant

With the foregoing criteria in mind, I have developed a screw-type implant. It is made of lucite which has proved to be non-irritating to tissue.[5] It is light and inexpensive.

A slightly elongated 18-mm. ball has muscle slots burred through it, as indicated in Figure 1. The face of the implant has a circular depression where the muscles come together and into which they drop after being sutured. The hole through the center of the implant is threaded to take a standard vitallium screw which has a squared and smoothed head.

Surgical technique

The surgical technique is similar to that employed for the insertion of the ordinary glass ball, with one exception. Before the recti muscles are cut, a 5-0 plain catgut suture is threaded through the tendon near its insertion and knotted at either edge of the tendon as indicated in Figure 2. This makes it possible to suture later the opposing tendons end to end and not pucker the ends and thus reduce their width (fig. 3). It is important to have the tendons spread out as wide as possible before dropping them into the depression.

After the rectus muscles are all separated

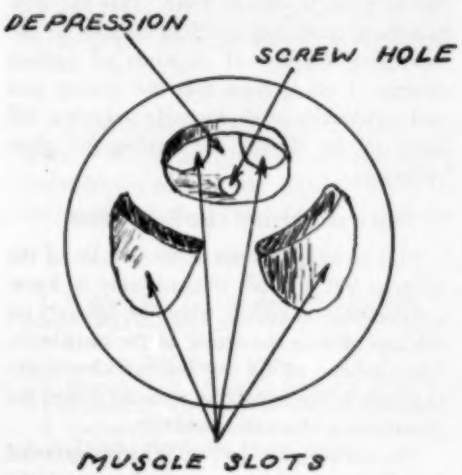

Fig. 1 (Moore). Side and top view of lucite implant.

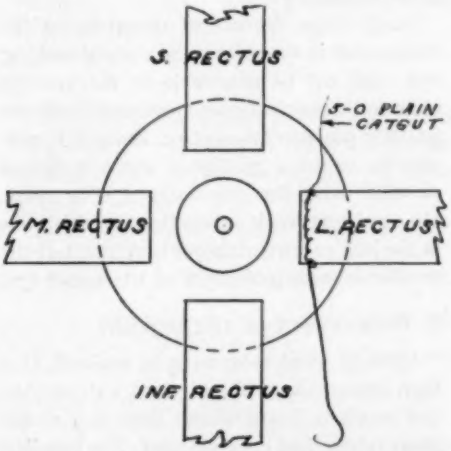

Fig. 2 (Moore). Diagram of rectus muscles. The plain catgut suture is inserted before separating the tendons from the globe to facilitate handling in the next step (fig. 3).

from the globe, Tenon's capsule is then investigated and carefully dissected from the recti leaving about 6.0 to 8.0 mm. of free tendon and muscle. This makes it possible to draw the tendons into the slots and not pucker or make taut Tenon's capsule when it is made to pursestring over the implant later in the procedure. This latter step may be done later but is easier at this time.

The oblique muscles are then cut and the globe is delivered. After the globe is delivered (I prefer the snare because of the satisfactory hemostasis), the sutures are threaded through the appropriate muscle slots and the opposing recti tendons are sutured with 5-0 chromic catgut (fig. 4).

When the first two opposing tendons are sutured, they are allowed to drop back into the muscle depression, and the remaining two tendons are then sutured. They, too, are allowed to drop back. Tenon's capsule is carefully pursestringed with 4-0 chromic gut. The conjunctiva is then closed with plain catgut.

There is always a fair amount of edema of the orbit, and sometimes of the lids, postoperatively. This lasts four or five days but does not prevent the patient from leaving the hospital on the second or third day. There is very little discharge. After the edema and congestion subside, there is a well-formed stump with a flattened anterior surface.

The cul-de-sacs are roomy if the conjunctiva has been used sparingly when sutured. A plastic conformer with holes in it should be placed in the conjunctival sac at operation to maintain further the cul-de-sacs. The conformer also prevents the sometimes edematous bulbar conjunctiva from evaginating through the palpebral fissure where it may become incarcerated and further reduce the depth of the cul-de-sacs.

Approximately 10 weeks after the enucleation, the tissues are healed and the screw can then be inserted. Children should be given a general anesthetic. If local anesthesia is the choice, very little two-percent procaine is needed. Injection of a small amount of the anesthetic in the center of the face of the stump and on either side deep into the horizontal rectus muscle slots is sufficient.

The implant is stabilized with a towel clip, the points of which barely enter the slots occupied by the horizontal recti. Little pressure is needed to keep the points of the towel clip inserted in the slots. Their presence prevents the implant from sinking in and rotating when the screw is inserted.

A knife needle is then thrust through all the tissues in the direction of the threaded

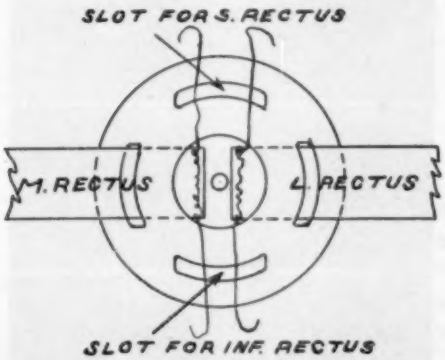

Fig. 3 (Moore). The tendons are in apposition after being drawn through the muscle slots of the implant. The previously placed plain catgut sutures facilitate the next step (fig. 4).

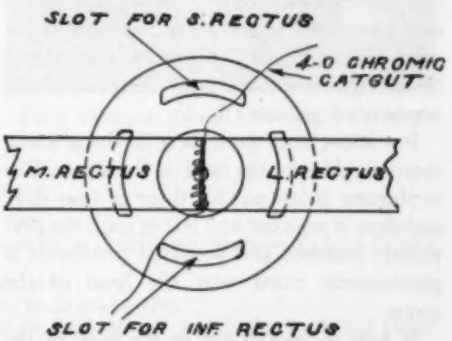

Fig. 4 (Moore). Diagram showing the ends of the tendons of the medial and lateral recti sutured together, sparing their full width, and dropped back into the muscle depression.

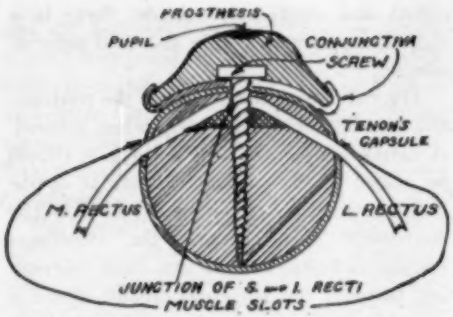

Fig. 5 (Moore). Diagram of cross section of implant after prosthesis has been fitted.

hole in the center. The knife is then used to enlarge the opening to accommodate the screw. The oozing of blood is stopped and the screw may be inserted but only after the direction of the screw hole is determined.

The screw is grasped with a ground-down optician's screw-driver, but small pliers may be used. It is turned backward until it engages in the tapped hole. Turning it backward allows a few turns in the hole before the soft tissues tighten around the screw. After each turn, forcing the screw into the hole with minimum pressure against the towel-clip points, the soft tissues are teased away from the screw with a dentist's pick or similar instrument.

No force should be used for fear of breaking the implant. None is necessary, if the soft tissues are teased away from the screw after each turn and if the screw gets started in the right direction. Only the head of the screw is left outside (fig. 5).

For about three days, there is edema which may conceal even the head of the screw. The conformer is left out for three or four days and then is replaced and left in until the previously matched and prepared prosthesis is permanently fitted over the head of the screw.

A hole is burred out in the back of the plastic prosthesis (any one of which will do) to house the head of the screw. The patient is instructed to use a drop of 30-percent sodium sulfacetimide once daily. Use of sulfacetimide may or may not be necessary for there is no more drainage than is found when a glass ball has been inserted.

Results

In 14 cases, operated in the past four years, the screw-type implant has been employed. Trauma resulted in enucleation of 10 eyes, and four were enucleated because of intraocular tumor. The average time the implant has been in place is 48 months. In

Fig. 6 (Moore). Case 1. Photographs showing movement of prosthesis (right eye).

no case is there a suggestion of retraction of the conjunctiva from around the screw. All cases were rechecked just before this paper was written.

Since the conjunctiva is adherent to the underlying Tenon's capsule and that in turn to the muscle mass in the muscle depression of the implant, no retraction is anticipated because the conjunctiva is merely adjacent to but not attached to foreign material.

Motion is excellent both as to excursion and in being instantaneous with the sound eye. Figures 6 and 7 show the movement in two of the 14 cases. Photographs are inadequate in showing instantaneous motion from primary position. In three cases there has been bilateral acute mucopurulent conjunctivitis with no effect on the implants. No cases have been troubled with discharge after the first three weeks postoperatively.

Summary

The criteria for a satisfactory implant have been enumerated. A new type of implant has been described which meets all of these criteria.

The problem of extrusion (none in this series) of retained and yet exposed foreign material is met by allowing the tissues to heal completely following the insertion of a lucite implant. The lucite implant (buried) has been used extensively in the past three years (Allen, Ellis, Landegger). The departure from what is becoming standard procedure occurs when the screw is inserted through the well-healed tissues.

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Fig. 7 (Moore). Case 4. Photographs showing movement of prosthesis (right eye).

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A SIMPLE CLASSIFICATION OF RETINAL ANGIOPATHY IN GENERAL ARTERIAL HYPERTENSION

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Since most clinicians realize that a fundus study provides the most reliable data for differentiation of the various types of hypertension, the ophthalmologist is frequently consulted by the internist concerning patients with general hypertension.

After he has been provided with data on the previous history and present condition of the patient, it is the ophthalmologist's task to make a careful, methodical ocular examination, studying systematically every detail of the eye condition. He must use every method of examination at his disposal, including such procedures as examination of the fundus in monochromatic light and retinographic documentation.

In my work in general hospitals in which both the medical and cardiac services use routine ophthalmic consultations, I endeavor to provide concise data based on two principles: (1) A simple classification and (2) determination of the grade of arteriosclerosis of the retina and choroid.

My study was begun in 1925 at a time when the exact nature of arterial hypertension had not yet been determined. I shall not attempt to review the numerous more or less complicated classifications which have been proposed during this period, for cumulative experience has taught me to appreciate the advantages of my own classification and has convinced me of its practicality.

Since it is now established that the vascular accidents which at any moment may modify the course and prognosis of hypertension are the results of the arteriosclerotic changes concomitant with the disease, the classification is based on grading the extent of the arterial hypertension by the degree of sclerosis of the blood vessels.

GRADES OF ANGIOPATHY

It is my opinion that the angiopathy found in malignant hypertension, from the incipient to the maximum, may be classified into three grades.

GRADE I. ARTERIOSCLEROSIS OF RETINA AND CHOROID

Vision. Usually normal.

Papilla. Generally, slight pallor of its middle sector; slight edema of its superior and inferior poles.

Retina. Moderate edema, most marked in the macular region.

Arterioles. (It should be understood that this term includes all the branches of the central retinal artery. The average diameter of 280 microns scarcely permits one to classify an arteriole as a small artery.)

The arterioles are in a state of increased tonicity manifested by a diminished caliber which reduces the normal proportion of arterioles to veins (2:3) to less than 2:3. This decrease in caliber is also termed the organic arteriolar constriction.

The central light reflex of the arteriole is increased because the pressure which the current of blood exerts on its walls straightens the vessel in such a manner that it is better

visualized in some sectors. This better visualization of the blood against the slightly altered vascular wall gives it an aspect known as the "copper wire."

Arteriovenous crossing. The arteriole does not permit the visualization of the column of blood in the underlying vein, indicating a fibrous connection between the two vessels, a fact which has been demonstrated anatomically.

Tonoscopy. Bailliart's ophthalmodynamometer reveals that the diastolic retinal pressure does not exceed half of the humeral diastolic pressure.

Grade II. Arteriosclerosis of retina and choroid

Vision. Central visual acuity is normal but the visual field has changes which are not typical. Usually there is a concentric contraction of the 1/1,000 isopter.

Papilla. There is diffuse pallor of the papilla due to a diminution or marked constriction of its precapillaries. This indicates a partial obstruction of the central artery the outline of which, when visible above the lamina cribrosa, is sharply outlined in red-free, sodium, or red-poor light. Frequently the poles of the papilla are blurred.

Retina. Generalized and localized edema, with gray peripapillary haze, obscure the borders of the papilla, especially on the nasal side. The nutritional changes in the retina are manifested by brilliant iridescent points, which are situated in the limitans interna (probably microscopic deposits of cholesterol), a few small white foci of lipoid degeneration in the cells of the granulous layers, and a discrete infiltration (albuminuric exudate).

At times there are small pigment foci (secretion of the pigment epithelium). Punctiform hemorrhages in the middle portion of the retina are not merely the result of diapedesis but are indicative of organic changes in the precapillaries. Small white points correspond to sections of the capillaries.

Arterioles. The arterioles present a marked tonic contraction, which makes their proportion to the veins 1.5:3; frequently there is irregularity in the caliber of the arteriolar wall, manifested by irregularity in the visible current of blood. In red-poor, red-free, or sodium light, one can see a thickening of the arterial wall (due to an albuminous infiltration), cells full of fatty granules, and arteriosclerotic processes without significant changes in the surrounding retina. The macular precapillaries are corkscrew in shape, caused by a thickening of their walls through hyaline degeneration.

Sometimes a fine, white glistening line is seen to accompany the arterioles and precapillaries and their branches in their entire course. In my opinion this is due to an accumulation of cholesterol in the limitans interna adjacent to the course of the vessels.

In some cases foci of angiospasm are seen peripapillary, or close to the papilla, predominantly in the first curve of the principal arterioles, the spastic sector being no longer than one third to one half the diameter of the papilla.

Monochromatic illumination enables one to see how the caliber of the vessel can contract without thickening of the arteriolar wall. The appearance of the arteriole known as "silver wire" may be encountered in isolated spots.

Arteriovenous crossings in this grade give the appearance of cut venules because there appears to be a white space on each side of the arteriole. It is actually the pathologic thickness of the arteriolar wall.

In the choroid one encounters vascular sclerosis which is easy to see because of the frequent diminution or atrophy of the pigment epithelium. With the arteriolar walls markedly sclerotic, the veins are intensely engorged. Sometimes they form large venous ampullae (up to 0.5 disc diameter), giving the aspect of a green spot.

Tonoscopy. The diastolic retinal arterial pressure is usually equal to or slightly higher than half the humeral pressure; this relation

is not constant and, in some cases, it does not run parallel to the general blood pressure.

According to Bailliart, ophthalmodynamometry measures the functional tonic arteriolar reaction, since it demonstrates the resistance of the walls of the retinal vessels to the current of blood. In the second grade of hypertension, the increase in the diastolic pressure indicates an increase in the tone of the arteriolar walls.

GRADE III. ARTERIOSCLEROSIS OF RETINA AND CHOROID

Vision. Vision is impaired and patients complain of spots and shadows in the fixation point and cloudiness. Objectively, central vision is much diminished; in some cases the absence of central fixation makes the taking of the visual fields difficult. When fields are obtainable, there is usually an enlargement of the blindspot and a uniform concentric contraction.

Papilla. There is frequently an optic neuritis, with slight or moderate edema. The swelling of the papilla may not exceed one diopter but the entire peripapillary sector is edematous. Or, it may be a frank edema of the papilla, in an intensity which varies from two to six diopters.

Retina. In some cases an intense diffuse edema, accompanied by a serous exudate in the external granular layer, obscures the details of the lesions in the internal retinal layers and completely obliterates those of the external layers, as well as the anatomic boundaries of the macula.

The spots in the retina are of various types: There are yellowish white, cotton-wool spots (due to lipoid degeneration), light white brilliant dots (posthemorrhagic fibrin), punctiform ischemic infarcts in the visible terminations of the precapillaries, and other punctiform spots along the nerve fibers. One may also encounter iridescent crystals (cholesterin); frequently there is a more or less complete macular star.

Hemorrhages of greater or less depth, are in or under the nerve fibers. They are of various shapes and sizes, old and fresh, with or without fibrin. There are also seen sectors of ischemia, corresponding to complete arteriolar obstruction, or to the most pronounced arteriovenous crossings.

Arterioles. The caliber of the arterioles is constricted, the tonic contraction is at its maximum, and there are numerous progressive angiospastic foci which give the vessels the appearance of rosaries. Many vessels have sectors of incomplete obstruction, occupying mostly the spaces at their bifurcation; these may be seen in the periphery, as long as the current of blood continues, even if it is narrowed, giving the appearance known as "silver" arterioles.

Angiospastic foci are characteristic of the cerebral vessels, the central retinal artery, and retinal arterioles. This fact was established experimentally by Riser, who produced localized spasms limited to the stimulated arterial segment without any effect on the vasomotor innervation.

Arteriovenous crossings are of the maximum grade and are characterized not only by the appearance of the venule cut by the overlying arteriole but also by that of the distal sector of the venule which is distended in an ampulliform manner and is sometimes hemorrhagic. The proximal sector is greatly constricted, and there are ischemic or hemorrhagic areas around it.

The apparent interruption in the course of the venule is most pronounced in the third grade of hypertension because frequently the hyaline degeneration of the arteriole is almost completely "silver wire." It is not unusual to find a crossing of double "copper wire" when the degeneration involves both vessels.

Tonoscopy. The diastolic pressure of the central retinal artery is elevated, approximating and sometimes equalling the pressure in the humeral artery. This frequently indicates a more or less marked intracranial hypertension, a state also called hypertension

encephalopathy. As previously reported, I have no difficulty in performing tonoscopy even in cases of frank edema of the papilla.

Comments

Grade I

In general, ophthalmoscopic changes at this stage are found in patients between 45 and 60 years of age, and this degree of hypertension is well tolerated. With appropriate therapy, more hygienic than medicinal, these patients, with few exceptions, live a long time. Albutt and Janeway lived under such conditions for over 20 years. Wagener and Keith reported on 37 cases of which only one developed a high hypertension (220/120 mm. Hg.), nine died of coronary disease, and the rest lived in good condition. We are in complete agreement with these two authors that the complications of arterial hypertension, including the retinal, are a manifestation of diffuse arteriolar angiopathy.

Grade II

Patients with changes in the second grade rarely consult the ophthalmologist because their visual symptoms are not significant and are rarely annoying subjectively. Functional inadequacy of some organs leads them to consult an internist who, finding advanced symptoms of hypertension (hypercholesterinemia, hypercoagulability, sometimes albuminuria, and so forth), requests an ophthalmic consultation. Usually these patients are over 50 years of age.

Because of the data found on ophthalmoscopic examination, general somatic examination, and cardiovascular examination with special attention to the coronary vessels ("study of retinal angiopathy in general hypertension in relation with coronary sclerosis"), I include in this classification practically all those cases which according to Wagener and Keith are in the third group.

In these cases the prognosis is serious. Generally the life expectancy is not over 10 years and the patients die within this period of cardiac or coronary disease.

In 30 percent of cases, vascular complications develop, such as obstruction of the central retinal vein, thrombosis or total occlusion of the central artery.

Grade III

Patients in this classification are considered to have malignant hypertension.

They consult the ophthalmologist because of serious ocular disturbances, irregular but constant. They are usually under 40 years of age and, according to statistics, they die early, not over one year after the ocular subjective symptoms appeared.

Conclusion

In conclusion, I propose this simple classification, evolved over a long period of observation, in the belief that, to be helpful to the internist, ophthalmic information should be concise and limited to what he can correlate with his own findings relative to the gravity of the disease, to the prognosis, and to the advisability of surgical intervention.

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NOTES, CASES, INSTRUMENTS

MACULAR PIGMENTATION FOLLOWING MATERNAL RUBELLA*

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The occurrence of congenital cataracts and other anomalies following German measles in the mother has become well known since Gregg's[1] original report in Australia in 1942. Other anomalies commonly described are cardiac abnormalities, deafness, and microcephaly. Isolated anomalies such as buphthalmos, microphthalmus, hypospadius, corneal opacities, and mental retardation are also mentioned.

Pigmentary changes in the retina are sporadically described in the literature. Four cases seen recently, in which practically the only ocular abnormality was a highly diagnostic pigmentary disturbance of the macula, stimulated this report.

CASE REPORTS

CASE 1

B. B. was born on September 9, 1943. This six-year-old white girl was told in school that her vision was defective. The mother stated that she held her reading material very close.

When the child was examined on November 16, 1949, the mother said that she had had rubella during the third month of her pregnancy. The infection was reported to the local health department.

Visual acuity was: R.E., 20/25; L.E., 20/30. External examination revealed nothing abnormal. The eyes were orthophoric on distant fixation, and a small amount of exophoria was present at near.

Refraction with homatropine was: R.E., +2.0D. sph. ⊂ +0.75D. cyl. ax. 45°; L.E., +2.0D. sph. ⊂ +1.0D. cyl. ax. 125°. This improved vision to 20/20, O.U.

The media in each eye were clear, there were no lens opacities. The right fundus was normal.

The left fundus showed a mottled black pigmentation at the posterior pole about four disc diameters in area, extending from the limits of the superior to inferior temporal vessels. The lesion was approximately circular extending to temporal edge of the optic disc, and the center of the lesion was in the macula.

The blotches of pigment were distinctly larger in the middle, about 1.5 vein diameters in size, of a slightly irregular round shape, decreasing gradually in size to the periphery of the lesion and fading into dustlike dots. Each pigment spot was fairly well demarcated and appeared to consist of tightly packed black granules.

The appearance of the retina and choroid between the pigmented spots was unaffected. The retinal vessels coursed superficially to the lesion and were normal in appearance in this area and the periphery of the retina. Both optic nerveheads were normal. No foveal reflex could be seen.

With a binocular ophthalmoscope, using Hildreth illumination, the pigmentation was only slightly discernible and appeared deep. This type of illumination does not penetrate the retinal tissue well, almost completely obscuring the pigment. With the ordinary ophthalmoscope, the lesion stood out sharply.

Reëxamination on September 5, 1950, revealed no changes in the vision or fundus appearances.

CASE 2

W. G. was born on October 8, 1943. This six-year-old white girl was seen on November 23, 1949, because of inadequate visual acuity discovered at school during a routine examination.

The mother had had rubella during the second month of gestation and the infection was reported to the health authorities. The patient had been born deaf, attributed to the maternal rubella by otolaryngologists. She was thin and rather short for her age.

The unaided visual acuity was: R.E., 20/50; L.E., 20/40, with the illiterate E chart. The eyes were orthophoric and convergence was within normal limits. External examination was not significant.

An atropine refraction revealed: R.E., −3.5D. sph. ⊂ +4.0D. cyl. ax. 5°; L.E., −4.0D. sph. ⊂ +4.5D. cyl. ax. 165°. The visual acuity was 20/30 in each eye with this correction.

The media in each eye were clear. There were no lens opacities. The optic nervehead was normal and the retinal vessels showed no abnormalities.

In the macular area, 1.0 to 1.5 disc diameters wide, somewhat horizontally oval with the macula as the center, was a pigmented area. The pigment was granular and blotchy; the larger pigment spots were in the macular area, about one vein diameter wide and decreasing uniformly to the edge of the lesion.

Within the foveal portion between the pigmented spots, depigmented areas were visible as a lighter

* From Department of Ophthalmology, Marquette University Medical School, and the Milwaukee Children's Hospital. Presented before the Chicago Ophthalmological Society, October, 1950.

pink color. This was more marked in the left eye. Reëxamination on August 30, 1950, showed no change in the pigmented area or in visual acuity.

CASE 3

W. E. A. was born on November 23, 1943. This seven-year-old white boy was first seen in the eye department of the Milwaukee Children's Hospital out-patient clinic on February 21, 1950. He had been treated in this hospital for convulsions in January, 1949, at which time a diagnosis of idiopathic epilepsy was based on a history of convulsions and a dysrhythmia noted on an electroencephalogram. The mother stated that she had had rubella during her first trimester of gestation.

Visual acuity, unaided was: R.E., 20/200; L.E., 20/20. Atropinization revealed a refractive error of: R.E., +5.0D. sph. ⊃ +1.0D. cyl. ax. 90°; L.E., +1.5D. sph. ⊃ +1.0D. cyl. ax. 90°, which did not improve his vision in the right eye. The eyes were orthophoric.

The media were clear in both eyes with no evidence of any lens opacities. The fundus of the right eye was normal.

The fundus of the left eye showed at the posterior pole pigmentation similar to that described in Cases 1 and 2. It extended from under the superior temporal to under the inferior temporal vessels.

The cardiac clinic reported a musical systolic murmur at the apex and medial to the apex. There was no diastolic murmur. The murmur disappeared when the patient was supine. The heart was considered to be normal with a functional murmur.

CASE 4

C. R. was born on December 3, 1942. This seven-year-old white girl was examined in the ear, nose, and throat clinic of the Milwaukee Children's Hospital on March 13, 1950. A nonprogressive deafness of a moderately severe degree, conductive in type, somewhat greater in the right ear, was found.

The mother had rubella at two and one-half months of her pregnancy, was quarantined for two weeks, and reported to the Health Department of the City of Milwaukee.

On March 17, 1950, the child was examined in the eye clinic. Unaided visual acuity was: R.E., 20/20; L.E., 20/20.

External examination revealed no abnormalities. The left fundus was normal. The right fundus showed the same macular pigmentation as described in the previous cases.

The periphery of the fundus was very blond and, in the inferior temporal quadrant of the right eye, the retina showed a uniformly diffuse, fine, dust-like pigmentation not present elswhere. In addition, there was a moderate number of somewhat larger scattered pigmented dots in this area.

This patient was seen again on October 17, 1950, with no changes in the fundus or visual acuity.

COMMENT

These four cases with proved maternal rubella illustrate that congenital anomalies occur when the infection is present during the first trimester of pregnancy. This has been confirmed by many authors. In two of these cases there was an associated profound deafness. No cardiac or other anomalies were found. There were no other related ocular findings.

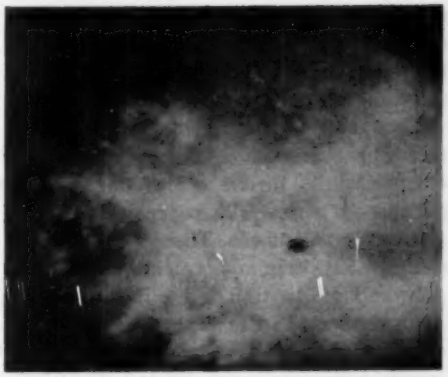

Fig. 1 (Blankstein and Feiman). Pigmentary changes of peculiar pattern and distribution in the macular area are typical of a maternal rubella infection. The macular area is on the left.

The amblyopia in Case 3 was considered refractive, because this eye did not show any pigmentary changes. Visual acuity was unaffected by the pigmentary change, nor was there any progression of the findings at later examinations. In two cases pigmentation was unilateral.

The pigment pattern and distribution were so identical in these cases (fig. 1) that the diagnosis of maternal rubella was made prior to questioning the mother. This was done from the ophthalmoscopic picture alone in the last two cases after our experience with the first two.

In no other disease has any approximate picture been described. The blotchy discrete pigment spots decreasing in size to the periphery of the area involved, are the outstanding characteristic. The pigment is deep in the retina, and its distribution creates an optical impression that the center is somewhat elevated. The foveal reflexes appear to be

absent. In Case 2, some depigmentation was noted in the foveal region, and in Case 4, there was some peripheral retinal involvement.

Long and Danielson[2] described "diffuse mottled pigmentation as though from a mild chorioretinitis" in one eye of three out of six cases reported with congenital cataracts from maternal rubella. These were the noncataractous eyes in each patient.

Swan,[3] of Australia, described "multiple small pigmented spots on the fundus" in one case. Prendergast[4] reported two cases of pigmented retina in a survey made in California in the fall of 1944.

Kyle,[5] in an ophthalmoscopic study of 30 cases of congenital heart disease, found the principal ocular manifestation to be directly proportional to the severity of the polycythemia. In no case could a history of maternal rubella be obtained. One patient, aged six years, showed a marked pigmentation of the macular areas in both eyes. He thought it might be a juvenile macular degeneration. Vision was 6/6 in both eyes. From the present knowledge it would seem most likely that the condition was due to maternal rubella, the skin and systemic manifestations having been so mild in the mother that they were ignored.

Walsh[6] describes a case with bilateral symmetrical retinal changes possibly best described as atypical retinitis pigmentosa. The vision seemed good.

Alarcon[7] quotes Franceschetti that among the deformities found in maternal rubella a pseudoretinitis pigmentosa exists. In discussing Goar's[8] presentation on congenital cataracts in maternal rubella, Cordes[9] describes two cases with clumped and scattered fine pigment particles throughout the fundus, most prominent in the foveal area. The pigment appeared to be primarily in the retina and in some places covered the retinal vessels. Except for the vessels the whole picture suggested retinitis pigmentosa.

Ellett,[10] in continuing the discussion of Goar's paper, described the left eye of a patient as pigmented as in congenital syphilis.

Terry[11] also noted pigmentary changes minute in size, similar in form and distribution to those of retinitis pigmentosa.

An examination of the congenitally deaf at the Blind and Deaf School in Brisbane by Marks[12] showed that of 38 children with a history of maternal rubella, 17 had abnormally pigmented fundi. Twenty-seven deaf children out of 101 examined had abnormal pigmented fundi. Of these 27, 21 had a maternal rubella history.

He mentions the fact that the absence of a history does not imply the absence of the disease because the illness is so mild. He describes the pigmentation as an atypical retinitis pigmentosa, not of the bone-corpuscle form but coarsely mottled, with normal blood vessels, and vision not affected sufficiently to interfere with school work.

In the discussion of his paper Gregg[13] credits Aileen Mitchell of Australia for the first observation of pigmentation of the retina in these cases. Gregg[13] found marked pigmentary changes in 16 cases out of 52. He feels that the picture is typical and has a distinctive appearance leading to a correct diagnosis. He describes the pigment as measly or blotchy, involving the macula and an area three to four disc diameters surrounding it. In a few cases there was a wider distribution. The spots of pigment were discrete.

The pathogenesis of the congenital cataracts appears to be related to the time the cells in active division are affected by the transmitted disease. Ida Mann[14] found a definite parallelism between the time of onset of the maternal infection and the known times of active proliferation of lenticular, cochlear, and cardiac primordia. This same theory may apply to the disturbance of the pigment epithelium of the retina. However, Swan,[15] in a histologic study of three infants dying from congenital defects following maternal rubella, reported normal retina, choroid, and optic nerve. The lenses were cataractous.

SUMMARY

Four cases with pigmentary changes in the macular area highly typical of a maternal rubella infection are reported. The distinctive appearance of the pigmentation is considered to be diagnostic of the disease.

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METHOD OF TREATING VITREOUS ADHESION TO CORNEA

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Collapse or tardy reformation of the anterior chamber following cataract extraction is not too unusual. However, the occurrence of a firm adhesion between the vitreous and the posterior surface of the cornea, after cataract removal, is less frequent. This is followed by irritation of the eye with often formidable sequelae.

Reese* has reported comprehensively on herniation of the hyaloid membrane and its treatment. Dunphy* discussed one case in which air was used to free a vitreous adhesion with good results.

This is a presentation of one case in which success was achieved by injection of air into the anterior chamber.

An intracapsular cataract extraction was performed on a 75-year-old woman on December 1, 1950. Corneoscleral sutures were used and the procedure was performed without incident; 24 hours later, at the first dressing, the anterior chamber had reformed.

The eye was dressed daily and the patient was discharged on the eighth postoperative day. At this time the anterior chamber was of normal depth and the eye quiet.

Three days later the patient was seen in the office with total loss of the anterior chamber but no evidence of leaking wound. No space could be seen between the vitreous and the posterior cornea. Near the center of the cornea was a pigment spot about one mm. in diameter.

A pressure dressing was applied and, about one week later, the anterior chamber began to reform slowly. At this time there was noted a firm adhesion of the vitreous to the posterior surface of the cornea at the site of the pigment deposit, causing the an-

* Reese, A. B.: Am. J. Ophth., 32:933, 1949. With a discussion by Dunphy, E. B.: Ibid., p. 940.

terior limiting membrane to be drawn up in the form of a cone.

For the next three weeks the eye became progressively more sensitive and a low-grade iritis continued. It, therefore, seemed necessary to attempt to sever the adhesion.

Using a small syringe and a hypodermic needle, air was injected into the anterior chamber in the following manner. The needle was introduced just anterior to the limbus and great care was taken to insure that the point did not touch the anterior limiting membrane of the vitreous.

Slight pressure was exerted on the plunger as the needle was pressed through the cornea. This enabled the operator to stop as soon as an air bubble appeared, thus assuring that only the very tip of the needle had entered. Air was then injected until the eye was quite hard. A few moments later on examination, the adhesion was seen to be severed.

When the air had become absorbed a few days later, the vitreous was well in place; the anterior limiting membrane was intact and lying flat behind the pupil and the uveitis had subsided. When the patient was last seen, three months postoperatively, the eye was quiet and corrected vision was 20/25.

611 City Building.

A NEW SYNERGISTIC MYDRIATIC COMBINATION*

A PRELIMINARY REPORT

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I was recently a member of a team assigned to study, and, if possible, prevent the blindness so often associated with the incidence of retrolental fibroplasia in the premature infant. This study entailed the careful and meticulous funduscopic examination of many premature infants. The schedule in a busy premature nursery would include examination of about six infants in one afternoon, of which about half would be reëxaminations so necessary in a careful follow-up study.

At the beginning of this study it became apparent that the greatest difficulty to be surmounted was the uncertainty experienced in the use of the available mydriatics. Many pupils would not dilate, or dilatation would stop at half-mydriasis. In an attempt to surmount this difficulty combinations of mydriatics were studied.

This is a preliminary report of a synergistic mydriatic combination that fulfills the following criteria believed to be of importance in the routine funduscopic examination of premature infants: (1) Rapidity of action; (2) certainty of action; (3) active with deeply pigmented irises; (4) relatively short duration of action; (5) no undesirable systemic side reactions.

THEORY

Epinephrine substitutes are sympathomimetic agents. The most important effect of these agents on the intraocular muscles are concerned with cells producing the effector substance in the iris dilator. This effect is reinforced by the ability of the same agents to affect cells in the opposing muscles which receive only inhibitor fibers from the sympathetic system. Thus, the iris sphincter partially relaxes under sympathetic stimulation, as does the ciliary muscle to a lesser extent.

Phenylephrine hydrochloride (neosynephrine hydrochloride) is stable for long periods even in high concentrations. The mydriasis produced is prompt and active and the effect on accommodation is definite but slight.[1]

Eucatropine hydrochloride is another drug classed as a sympathomimetic agent. The mode of action is different but it is synergistic to the epinephrine substitutes in that eucatropine (and cocaine) sensitizes the muscle cells to the action of sympathin and

* From the Department of Ophthalmology, The Jewish Hospital of Brooklyn.

the epinephrinelike compounds. Moderately active mydriasis is produced with a slight decrease in accommodation. The duration of action is relatively brief.[1]

Theoretically, a mixture containing phenylephrine and eucatropine should be synergistic to a remarkable degree; eucatropine sensitizes the iris dilator to the action of phenylephrine.

To complete this synergistic mixture it was incorporated in a one-percent methylcellulose solution.[2, 3] This is a high viscosity, emollient solution, colorless and odorless, which mixes well with secretions. It spreads smoothly throughout the conjunctival sac.

The resultant mydriasis is smooth and uniform. The high viscosity properties of this substance enables the mydriatic mixture to remain in contact with the bulbar conjunctiva and cornea for a longer period of time. The instillation of eyedrops in infants is a difficult procedure to say the least. This high viscosity solution results in retention of medication in the conjunctival sac despite crying and the profuse production of tears.

Materials*

The mydriatic combination utilized contained five-percent phenylephrine hydrochloride, five-percent eucatropine hydrochloride, one-percent methyl cellulose, in a diluent of 0.45-percent sodium chloride. This solution remains stable for at least two months. Slight discoloration due to the oxidation of the phenylephrine does not detract from the mydriatic properties. Marked discoloration results in a highly irritating solution, but does not occur before two months of storage. The presence of eucatropine appears to preserve the phenylephrine, since similar solutions of phenylephrine without eucatropine become markedly discolored in about one month.

Results

An unselected group of 75 premature infants was utilized. They varied in birth weight from 2.5 to 4.5 pounds. There were 20 Negro infants in the group. One drop of the mydriatic mixture was instilled by the ward nurse every 15 minutes for three doses. Maximal mydriasis was achieved in every case one-half hour following the third instillation. No side reactions were observed. The duration of action varied between four to six hours. In almost every case the pupils were back to normal with good pupillary light reflexes in six hours.

Similar results were achieved in an unselected group of 100 adults. In the average case, one drop of the mydriatic mixture gave maximal dilatation in one hour with the duration of action lasting four hours. No systemic or local side reactions were noted. There was no notable increase in intraocular pressure. The solution appears to be slightly less irritating than the 10-percent solution of phenylephrine hydrochloride in common use.

Summary

A new synergistic mydriatic combination is presented which is of great value in the ophthalmoscopic study of the fundus oculi of the premature infant. It offers advantages unobtainable with the mydriatics now available. Preliminary study disclosed the following advantages: rapidity and certainty of action with both deeply pigmented and nonpigmented irises, relatively short duration of action, and no undesirable systemic side reactions.

434 Beach 123 Street.

* Kindly supplied by Robert S. Feinstein, 1315 48th Street, Brooklyn 19, New York.

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COVERED WAND FOR TEST OBJECTS

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Subjective testing in any field is at best uncertain. With the tangent screen, a few test objects, and two human beings—the patient and examiner—these uncertainties easily become evident. Therefore, it appears that any device which will decrease extraneous factors and annoyances should be valuable.

Dissatisfied because the flat test objects made of wire and paper soiled easily, nor were the test objects small enough, I ordered a set of Berens spherical test objects which are attached to separate pins. These pins may be inserted into either end of a black wand included in the set. The colored test objects are as small as 2.0 mm. in diameter and the white 0.5 mm.

They are very satisfactory test objects. But use showed that I had exchanged one annoyance for another. A light reflex came from the wand and even a little reflection came from the pin which bears the test object.

Using the 0.5-mm. or 1.0-mm. white test objects at one or two meters, these light reflexes are extremely disconcerting to the patient. With colored test objects they are even more so.

To abolish these reflexes, I have devised a cover long enough to enclose both wand and pin. Made from a piece of black felt about 10.5 by 1.5 inches, it is simply rolled lengthwise, a slightly exasperating task, but an electric iron and an assistant will help. It is then sewed with black thread after it is rolled. Since the cover is considerably longer than the wand, it may be difficult to recover the wand once it disappears in the cover. However, an applicator stick constantly at hand can be used to push it out.

With this covering, no light reflex gleams from the wand or the pin. The felt cover is pushed up to the test object. While this may not be so important when large targets are used, it becomes quite noticeable to the patient when 1.0-mm. and 0.5-mm. white and colored test objects are used.

1765 Sherman Street (5).

STREPTOMYCIN IN MILIARY CHOROIDAL TUBERCULOSIS

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The subject of tubercles of the choroid receives an excellent historical review by Illingsworth and Wright.[1] In addition, they describe the frequency, the natural history, and the results in the treatment of the tubercle choroid with streptomycin.

Mejer[2] observed choroidal tubercles in the fundi of children with tuberculous meningitis and miliary pulmonary tuberculosis treated with streptomycin: "in the majority of children resolution of foci was rapid after the initiation of the treatment with streptomycin, and the course of the disease was as a rule favorable."

I[3] reported a case of miliary choroidal tuberculosis in a patient with miliary pulmonary tuberculosis that was treated with streptomycin. It is the purpose of this paper to present a follow-up report of this case, and to describe an additional one.

REPORT OF CASES

Case 1. This case was seen on August 9, 1947. Ophthalmoscopy of the right eye showed five small, pinpoint, gray-white nodules. Three of these nodules were 2.5 disc diameters from the disc at the 1-o'clock meridian; two were at the 6-o'clock meridian.

Streptomycin therapy was instituted and continued for a period of three months. At the end of the third month, the choroidal tubercles at the 1-o'clock meridian had completely disappeared and those at the 6-o'clock meridian were scarcely perceptible.

This patient was last seen in August,

1948. There were no residual evidences of the nodules at the 1-o'clock meridian. Those at the 6-o'clock area were round with sharp margins and parchment white in color; pigmentation was not observed.

Case 2. T. C. was first seen on June 19, 1948. The diagnosis was miliary pulmonary tuberculosis.

Ocular examination of the right eye revealed a small, round, gray-white area, about 0.20 the size of the disc—approximately 2.5 disc diameters—at the 12-o'clock meridian. In the left eye, within 2.5 disc diameters of the papilla, there were two areas—at the 8-o'clock meridian, one-third disc diameter in size, and at the 7-o'clock meridian, 0.5 disc diameter in size. Both areas were round, slightly elevated, underneath large blood vessels, with no evidences of pigmentation, and with margins that were not sharply defined.

Streptomycin, one gm. daily in subdivided doses for a period of 84 days, was given. At the end of this period, in the right eye the lesion became atrophic, white in color, with sharply defined margins and with a small amount of pigmentation. In the left eye, the large lesions became flat, atrophic, parchment white, but with no pigmentary changes.

This patient was last seen on July 26, 1949. The pulmonary condition had cleared completely. The ocular findings were essentially the same except for slight pigmentary areas at the margins of the lesions in the atrophic areas of the right eye.

Comment

As previously reported, the course of miliary choroidal tubercles is altered and arrested by streptomycin therapy. Since roentgenograms of the chest may not reveal miliary tuberculosis, especially in cases of tuberculous meningitis, the presence of choroidal tubercles are of diagnostic[1] significance. It has been also suggested[1] that further studies may reveal the changes to be of prognostic value.

1330 Union Street.

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A SIMPLE INSTRUMENT FOR EXPLANATION OF STURM'S CONOID

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San Pedro, California

Because of the inherent difficulty in teaching students a subject which requires three dimensions to illustrate, when by drawings and diagrams only two are available, the subject of the conoid of Sturm and its associated uses is always hard for students to grasp.

Very often the instructor, who is attempting to lecture on the path of light rays through a cylindrical lens or on the value of the fogging technique in refraction, becomes so engrossed in whether the horizontal or vertical line is astride the retina that the class is lost in a maze of plus and minus. Moreover, it is quite useful, when speaking before lay groups, to have at one's disposal

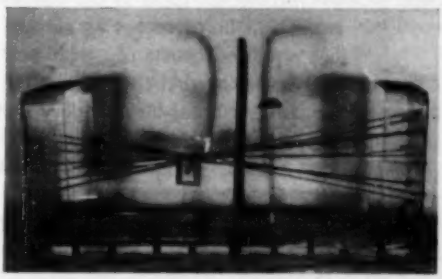

Fig. 1 (Zugsmith). Instrument for explanation of Sturm's conoid.

a device to show the pathways of light, the focus of light rays in emmetropic, hypermetropic, and myopic eyes, as well as in the astigmatic eye.

An instrument similar to that pictured in Figure 1 was constructed of wood and used by Dr. Arthur Jampolsky in his lectures at Stanford University, but it was reasoned that constructing the device of plastic would serve to make it completely three dimensional.

Dr. Irving Puntenny suggested putting on the machine the arbitrary marks which might be used for dioptric or other measurements. This was done and the instrument in its present form was found to be completely satisfactory for teaching and illustration.

The base was made of lucite in three pieces, the top two having a bevel forming a groove which holds in place a rectangular lucite button. This can be moved horizontally. Lucite rod was used as the guide for the vertical and horizontal lines.

The "retina" was made of 0.25-inch plastic rod, placed in the center of the machine and painted red. The light rays were constructed of piano wire and fixed at one end of the machine to the plastic box representing the cornea.

Sandwich boxes were used for both ends and they also prevent the plastic button from leaving the groove.

The wire "light" rays were painted in pairs in different colors. They are stiff enough to assume the exact pattern of light rays when the horizontal and vertical "lines" are moved.

All the materials are procurable from any hobby shop which carries plastic, and the effort put forth in constructing the device is well repaid by the interest shown by the students who see it, as well as by those interested in teaching.

529 West Eighth Street.

Ophthalmic Miniature

I have been engaged for several years investigating the subject of squint, and have made detailed notes of more than 1,800 cases. One of the results of this inquiry—is to prove conclusively that congenital amblyopia is very rare, and that at the first appearance of a squint the corrected vision of the deviating eye is almost as good as that of its fellow. . . . On seeing a case, therefore, one's first thought should be directed to the preservation of the sight of the squinting eye. This is to be accomplished by forcing the child to use this eye. Any refractive error should at the same time be corrected by glasses. . . . Yet when one sees a patient who has squinted constantly with one eye for a considerable time and has merely received the usual routine treatment, one usually finds that the deviating eye has become very blind.

Claud Worth,

British Medical Journal, September 26, 1903, page 732.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

April 19, 1951

DR. WILFRED E. FRY, *chairman*

ISOLATED BILATERAL ABDUCENS PALSY

DR. ROBERT A. GROFF and (by invitation) DR. HAROLD ROSEGAY said that bilateral paralysis of the abducens nerve is caused by various etiologic processes which can be conveniently divided into two groups.

The first and larger of the two is caused by direct involvement of the nucleus in the brain stem and/or the nerve by specific pathologic entities such as a toxin, inflammation, or neoplastic process. In each of these, there is, in addition to the bilateral abducens palsy, a number of additional neurologic signs because of the involvement of neighboring structures.

Examples of diseases in this group are diabetes, myasthenia gravis, pontine tumors, multiple sclerosis, measles and mumps, encephalomyelitis, encephalitis lethargica, bilateral Gradenigo's syndrome, lateral sinus thrombophlebitis, basilar meningitis, syphilis, nasopharyngeal carcinoma, and lymphatic leukemia. Congenital abducens and facial palsies are seen in Moebius' syndrome or facial diplegia.

The second group consists of those patients who have an isolated paralysis of both abducens nerves. The mechanism is either by stretch or by traction upon the nerves secondary to dislocation of the brainstem. Obviously, this is rare. The vulnerable portion of the nerve is between the point at which it leaves the brainstem and the point at which it enters the dura to traverse the wall of the cavernous sinus. Dislocation of the brainstem posteriorly either by trauma or tumor would readily affect this portion of the nerve.

Cases of isolated abducens nerve palsy have been reported in patients following cranial trauma, lumbar puncture, and in some lesions of the posterior fossa. Bilateral abducens traction palsy may also occur as a late and remote effect of brain tumor with increased intracranial pressure.

A case of isolated bilateral abducens palsy due to an interpeduncular teratoid tumor was presented. It was presumed to represent the stretch type of abducens palsy.

Discussion. Dr. Robert A. Groff: Dr. Rosegay has presented a rather unusual cause for bilateral sixth-nerve palsy.

This patient was sent to us as a possible case of brain tumor with the only symptom, double vision. On examination, she presented a bilateral sixth-nerve palsy and some curious nystagmoid movements about which Dr. Spaeth will have something to say. At operation, we saw no evidence of tumor, and had the rather startling experience of causing respirations to stop when the lower left side of the medulla was being inspected. At autopsy, the unusual location of the tumor was revealed in the interpeduncular space.

Dr. Rosegay's explanation of the nerves being stretched by the tumor and the curious course of those nerves gives plausible explanation for the paralysis of those nerves. I understand that this explanation had been made many years ago.

Dr. Edmund B. Spaeth: There is one other thing I want to mention; in spite of the bilateral sixth-nerve palsy, horizontal nystagmus and vertical nystagmus were present. It was rather interesting to see a nystagmus plus the palsy which this patient had only as the nystagmus appeared from the position of the paralytic convergence in contralateral rotation up to the midline. Then the cessation of movement, because of palsy,

but the continuation at that position of the nystagmus to the left or right. It was just a bit unusual to see it.

Dr. Francis Heed Adler: Two years ago a patient was brought in to see me with a condition I diagnosed at the time as a comitant squint, and which turned out to be a bilateral sixth-nerve palsy. This patient, a girl, aged eight years, was brought into the office with a history of having had a convergent squint for some years, and was referred by an uncle whom I had seen in the office several months previously with an old lateral rectus muscle palsy.

On examination the child showed what was thought to be a comitant squint, although the abduction of each eye was not complete. The possibility of a lateral rectus muscle palsy was ignored at the time. The child had a hyperopia of approximately three diopters, and some blurring of the discs, which was thought to be a pseudoneuritis. She was given glasses and treated as a comitant accommodative squint without any improvement.

During the next three months, it was noted that the blurring of the disc margins was increasing, and the child was complaining of increasing headache, finally accompanied by nausea and vomiting. It was then realized that the pseudoneuritis was the beginning of a true choked disc, and the child was finally admitted to the University Hospital as a suspected case of brain tumor. She was operated on and found to have a glioma from which she subsequently died.

The point I wish to make is that a bilateral lateral rectus palsy, if equal on the two sides, can give rise to a picture which simulates a comitant squint, and if, as in this case, there is a history of squint in the family and other signs usually seen in accommodative convergent squint, the true nature of the condition can be overlooked.

Dr. Glen G. Gibson: I think we are very indebted to Dr. Rosegay for bringing us this very instructive neuro-ophthalmologic case report. He has illustrated, first of all, that many of the signs in neuro-ophthalmology are unreliable for the localization of lesions. The number one, unreliable localizing sign is sixth-nerve paresis. This is equally true whether it is unilateral or bilateral. When we have a sixth-nerve paresis, which is not associated with other signs, we are frequently at a loss to localize the lesion, since it may be due to remote pressure or stretching.

Dr. Groff was extremely unfortunate to have a patient with an interpeduncular lesion with no signs of an interpeduncular lesion which, classically, shows bilateral third-nerve paresis and bilateral pyramidal-tract signs together with chiasmal involvement. This patient had none of these symptoms. The preoperative diagnosis in this case is difficult to understand, and I should like to ask the authors why, in a case of bilateral sixth-nerve paresis, they would think of an intermedullary lesion or a vascular lesion in the pons.

In such a case it would be quite likely that there would be pyramidal-tract signs or other evidence of intramedullary involvement. Would there not, Dr. Groff?

Dr. Robert A. Groff: Usually, yes.

Dr. Glen G. Gibson: This, of course, is a very unusual case, and a very difficult one, and that is just one other reason why we are very indebted to the authors for presenting this instructive case.

The most common cause of bilateral sixth-nerve paresis, which I have encountered, is nasopharyngeal malignancy, which always should be ruled out. This lesion was in exactly the place where you would expect a nasopharyngeal malignancy to penetrate, the base of the skull.

Another condition which is considered as a common cause of bilateral sixth-nerve paralysis is craniopharyngioma. In the past 20 years, I have seen only one case of craniopharyngioma which was associated with bilateral abducens paralysis.

Some years ago when the diagnosis of brain tumor was made later in the course of

the disease than it is today, it was a fairly common experience to encounter cases with bilateral sixth-nerve paralysis associated with increased intracranial pressure. No localizing significance could be attached to it. I note that the authors were very careful to state that there was no increased intracranial pressure in their case.

Dr. Harold Rosegay: The diagnosis of pontine glioma, of course, would be untenable. We rather had in mind a meningioma en plaque under the pons against the clivus. That is what I meant by pontine tumor. As for a vascular thrombosis, that is unlikely too, and we discussed the possibility of there being a repetition of Dandy's case of aneurysm of the vertebral artery, because our patient did have a sudden onset of diplopia, and had the isolated abducens palsy.

Aspiration biopsy of malignant melanoma of choroid

Dr. M. Luther Kauffman presented a patient with severe retinopathy in the left eye, complicated by angiosclerosis and diabetes mellitus. He had only 1/60 vision in this eye. The right eye had a large suspicious-looking lesion just above the macula, extending far into the vitreous.

In the vain hope that this might be benign, a biopsy was done by inserting a lumbar puncture needle into the globe behind the equator above the external rectus tendon and across the vitreous into the lesion. The stilette was withdrawn, negative pressure was applied to the needle, and material was withdrawn with the needle.

Malignant cells were demonstrated, and the eye was enucleated. A melanoma of low-degree malignancy was revealed at the final pathologic study. The man died nine months later of a cerebrovascular accident, with no manifest metastasis or local recurrence.

Discussion. Dr. A. D. Wallis: This case is an extremely unusual, if not unique, example of the increasing use of spreads or smears of cells in the diagnosis of malignancy. The usual criteria that we rely on in most examinations of this sort, as for example the common smears of vaginal and bronchial secretions, could not be depended on in this case.

As you know, nuclear changes are the basis on which we decide. The nucleus must be markedly enlarged or markedly hyperchromatic, or both, to recognize a malignant cell. In some tumors, as in the present instance, nuclei are quite uniform. So in this case, we had to rely heavily on circumstantial evidence.

May I have the first slide (showing first slide). This is a smear made at the operating table. The cells, as you can see, are often polygonal. The nuclei at this moment to me look far more variable than they did under the microscope. In some fields there were cells which were definitely pigmented.

Knowing that there was a mass, knowing that we found cells of a type which we normally do not expect in the retina, particularly accompanied by pigment, we concluded that there was in all probability a malignant melanoma.

The next slide (showing second slide). This is a section of the tumor after enucleation. It shows the uniform cell type, which is polygonal with a fair-sized not deep staining nucleus, very little vascularity, and considerable pigment in irregular distribution. This tumor can be classified as an example of the spindle-cell Type A of Callender, which is the least malignant of the melanomas of the choroid.

Among the peculiarities of these tumors, as you know, are their tendency to assume a dumb-bell shape, their rarity in the Negro (which as far as I know has never been explained), the infrequency of local extension in the orbit, their radio resistance, and, particularly, the late occurrence of metastasis, in some cases many years after enucleation. I think a case was reported in which death occurred 19 years after enucleation.

Dr. Kauffman and I were discussing the use of the term leukosarcoma for melanomas which are without pigment, and apparently

this is an accepted term in your specialty. To a pathologist, it is not a very happy term. I am not sure how to classify these tumors. Are they carcinoma or sarcoma? We are up against the same difficulty in the case of melanomas of the skin. There are two schools of thought. I would prefer to speak of those without pigment as amelanotic melanomas.

Dr. William Zentmayer: Some years ago I had an experience at Wills Hospital that raised in my mind the question whether aspiration is a safe procedure. Of course what occurred may have been a coincidence. A boy was seen with a suspicious detachment of the retina. Aspiration was done. I do not remember whether we were able to make a diagnosis from the procedure. The eye was enucleated, and a few months later a melanoma developed in the orbit, and I always felt that the orbital growth was metastatic as a result of the aspiration as the choroid was the seat of a malignant melanoma.

Dr. James S. Shipman: I am grateful to Dr. Kauffman for bringing this case before us. I am also grateful to Dr. Zentmayer for making the remarks that he has made, because he had deterred me on two or three different occasions from doing this procedure. However, on three different occasions when I could not get Dr. Zentmayer to look at the case, and we were not sure of the diagnosis, we have followed this procedure before doing a retinal detachment operation.

This was in cases in which there was doubt as to whether the detachment was serous or solid, and on none of the three cases in which we did this were we able to demonstrate any tumor cells. We proceeded with the electrocoagulation surgery, and were able to get the retina back in place. I mention this experience to emphasize the fact that this procedure, when it is positive is positive, but when it is negative, it is not necessarily negative.

Dr. M. Luther Kaffman: I wish to thank the discussors; to reiterate that we do not suggest this as a regular procedure, and that we are fully aware of the dangers of spreading tumor seeds along the tract. If this patient had not had as little as 1/60 vision in the other eye, it probably would not have been considered as a desirable procedure at all.

Dibenamine

Dr. Samuel L. DeLong (by invitation) and Dr. Harold G. Scheie presented a clinical and experimental study on dibenamine* which is a highly specific and potent sympatholytic and adrenolytic drug which blocks the excitatory effects of adrenergic stimuli. It has no significant cardiovascular effects except a marked orthostatic hypotension with tachycardia. It does not affect blood pressure of animals or normal man.

In five eyes of four patients with acute glaucoma, its administration caused a significant reduction in intraocular pressure in three eyes, a questionable reduction in one, and no effect in one.

In diffusion experiments on animals, dibenamine gave rise to no significant alteration in the amounts of systemically administered substances recovered in aqueous. Sodium fluorescein was found to appear in the anterior chamber at irregular and inconstant intervals, so that results were considered inconclusive. Only negligible amounts of inulin were recovered in aqueous of control and dibenamized animals. The amount of systemically administered para-amino hippurate appearing in aqueous was not appreciably changed after administration of dibenamine.

Changes in the rate of flow of aqueous from eyes under constant but slightly below normal pressure were then investigated. Animals showed prompt and significant decreases in rates of aqueous flow following administration of dibenamine, while rates of flow in control animals remained constant or increased.

* Supplied by Smith, Kline & French Laboratories.

In control animals after aspiration of aqueous and replacement with air, the intraocular pressure was shown to rise to levels far greater than normal and remain at these levels for five hours or over.

In experimental series it was definitely demonstrated that the levels to which the tensions rose were significantly lowered in animals which had previously received dibenamine. Further, when dibenamine was administered to animals after the "air-block glaucoma" had fully developed, prompt and significant decreases in intraocular pressure were noted.

The authors conclude that dibenamine is effective in reducing elevated ocular tension in man and animals, probably by its sympatholytic properties which in some way inhibit the secretion of aqueous.

Discussion. Dr. Harold G. Scheie: Dr. DeLong has mentioned that dibenamine is sympatholytic, blocking the effects of sympathetic stimulation. He also has presented evidence which confirms its effect in lowering elevated ocular tension in man and animals as well. He suggested that it acts through inhibiting the production of aqueous.

This was supported somewhat by the aqueous-flow experiments which he citied, as well as by the fact that, in man and in experimental animals, abnormally elevated ocular tension could be reduced by the administration of dibenamine, and in animals, an induced rise was never as high in eyes of dibenamine animals as in control animals. The elevated pressure in animals was presumably mechanical, due to obstruction of outflow of aqueous, and for that reason dibenamine should have exerted its effect by lowering the peak level to which aqueous could be secreted into the eye.

Because the effect of dibenamine in reducing ocular tension cannot be correlated with changes in blood pressure, a local ocular action is the most likely explanation. Several possibilities have been suggested or come to mind.

1. Swan showed that it was not related to an effect upon the intraocular muscles, because there is no relationship between pupillary size and its effect on tension.

2. It is also possible that dibenamine might affect the osmotic relationships between the plasma and intraocular fluids drawing fluid from the eye, but there is no evidence to indicate this.

3. The most likely possibilities remaining are those which tie in with the evidence presented by Dr. DeLong, that is, some effect upon aqueous flow.

(a) This could be brought about by changes in capillary pressure and permeability even though the systemic blood pressure had not changed. In our experiments, we found no evidence to indicate significant change in permeability of the blood aqueous barrier. It tended to support, instead, Friedenwald's hypothesis that epinephrine plays a role in the mechanism of aqueous production and that somehow this action is blocked by dibenamine. At any rate, the only positive evidence which we found in our experiments was that pointing toward diminished production of aqueous.

M. Luther Kauffman,
Clerk.

COLORADO OPHTHALMOLOGICAL SOCIETY

December 16, 1950

Dr. John C. Long, *presiding*

Sympathetic ophthalmia

Dr. Homer Cowan, resident in ophthalmology, University of Colorado Medical Center, presented a 65-year-old woman who gave a history of diabetes mellitus of one year's duration. This condition is controlled with 40 units of P.Z. insulin daily.

In April, 1949, she had had an extracapsular lens extraction followed by postoperative glaucoma and iridocyclitis. This

had been eventually controlled by atropine, heat, and foreign protein, although it dragged out over a long period of time.

In July, 1950, uveitis with glaucoma developed in the right, unoperated eye. This failed to respond to hospitalization and the usual treatment including antibiotics and sulfa drugs but did clear with intramuscular and topical cortisone.

Ten days after discharge from the hospital, while still using cortisone eyedrops, the uveitis and glaucoma returned. This recurrence did not respond to any kind of treatment so a basal iridectomy was performed on this right eye on November 3, 1950.

After this operation the patient did well on miotic therapy for several weeks, then the whole process recurred. During all this time, the left eye has remained quiet. Tension is now, R.E., 48 mm. Hg (Schiøtz); L.E., 23 mm. Hg. Vision is hand movements in each eye.

Recently uveal pigment was injected into the skin. The following biopsy showed that considerable pigment had been phagocytized. It was felt that this was a case of sympathetic ophthalmia. Further cortisone therapy with careful watch over the diabetes was recommended.

Possible allergy to sawdust

Dr. Montimore Shwayder presented a 30-year-old man who, after working in a sawmill, found his right eye red and swollen.

When first examined in October, 1950, corrected vision was 20/20, O.U. There was marked swelling of both right lids, chemosis, and some proptosis. The preauricular glands were enlarged. Pupils, ocular movements, fundi, and fields were normal.

In a week the proptosis increased and a mass was palpable in the outer angle of the lower lid. The patient was hospitalized for study.

Blood examination showed a six- to seven-percent eosinophilia. All antigen tests were negative. There was an enlargement of the inguinal, axillary, submental, and preauricular glands. The spleen was palpable.

Chest, skull, and orbit X-ray films were negative. On biopsy an inguinal gland showed hyperplasia and subacute inflammation, no lymphoma.

Dr. Joseph Kafka suggested obtaining some sawdust from the mill for a patch test. It was the consensus that bone-marrow studies and stool cultures should be made and that the orbit should be treated by X-ray radiation.

Keratoconjunctivitis

Dr. Harry Shankel presented a 25-year-old woman who for two weeks had had an infection in the right eye. This had started with swelling of the upper lid and had become progressively worse in spite of treatment. When seen at this meeting, the right lids were swollen with a subacute chalazion noticeable in the upper lid.

The palpebral conjunctiva was markedly injected and beefy. The bulbar conjunctiva was moderately congested. There was no pain, soreness, or photophobia; only a sense of burning.

Treatment had consisted principally of penicillin drops, sulfa drops, and penicillin injections before the patient consulted Dr. Shankel. Dr. James Strong said he felt this should be considered a case of epidemic keratoconjunctivitis. He had had, in a similar case, good results with cortisone drops.

Dendritic corneal ulcer

Dr. Walter Ohmart presented a 42-year-old man whom he had first seen six days earlier. This patient had a dendritic corneal ulcer of the right eye which had had repeated iodine and silver-nitrate cauterizations. The ulcer had healed and broken down again each time.

Dr. Leonard Swigert suggested 0.5-percent solution of methylene blue applied every hour. Dr. John Egan suggested the thermophore. Dr. William Bane recommended curettage for possible foreign body since the

symptoms began while on a hunting trip. Dr. Morris Kaplan and Dr. Daniel Franklin mentioned the use of hydrosulphosol.

Retinal detachment

Dr. John C. Long presented a 40-year-old woman who had been given a diagnosis of retinal detachment, right eye, four years ago. In spite of a practically total detachment, with a disinsertion in the superior temporal quadrant, surgery had brought about an anatomic cure with marked improvement in the visual field. There were extensive macular changes. Vision was 2/60.

Homogenous vitreous haze

Dr. Edward Swets presented an 11-year-old girl who had had poor vision since June, 1950. Examination showed bilateral homogenous vitreous haze and an increase in density of the aqueous ray in the right eye. Vision was 20/100 and 20/70.

Careful medical survey with chest X-ray and blood studies was negative. A Mantoux test was not done for fear of stirring up more trouble in the vitreous. Dr. George Filmer stated that many similar cases had been seen at Fitzsimons Army Hospital. They had been treated by everything in the book and X-ray radiation seemed to be the only helpful procedure. He suggested using half the dosage recommended by Guyton.

Subretinal hemorrhage

Dr. James Strong showed a man who had been struck in the right eye with a puck while watching a hockey game. He had developed a subretinal hemorrhage near the disc which was at first round, discrete, and elevated two diopters and had looked originally very much like a melanoma.

Sympathetic ophthalmia

Dr. Ivan Hix, Jr., resident in ophthalmology at the University of Colorado Medical Center, presented a six-year-old girl who had been struck in the left eye with an arrow on September 1, 1950. This eye had undergone progressive degeneration to a beginning phthisis bulbi with no light perception by December 1, 1950.

At this time the right eye began to show signs of inflammation with photophobia, cells, and aqueous flare. The left eye was forthwith enucleated. The right eye has been controlled and is now showing only a few cells in the aqueous under cortisone therapy.

Thomas M. Van Bergen,
Recorder.

Ophthalmic Miniature

Public opinion, which on medical subjects is generally erroneous, although for the most part founded on professional authority, is in no instance more injurious than in relation to the eye. It pronounces it to be an organ of a very delicate nature, exquisitely sensible, requiring the greatest delicacy of touch, and the utmost nicety of management; which opinion some oculists formerly found it convenient to support.

Guthrie, *Lectures of the Operative Surgery of the Eye*, 1830.

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THE PUZZLE OF RETROLENTAL FIBROPLASIA

Three important and highly significant papers on the fascinating though tragic problem of retrolental fibroplasia are to be found in this issue of the JOURNAL. The one by T. S. Szewczyk is an elaboration of his preliminary report published in the December, 1951, issue of the JOURNAL, and establishes, with some pertinent evidence, his thesis that anoxia plays a major role in the production of this mysterious disease.

The second, by T. H. Ingalls, C. G. Tedeschi, and M. M. Helpern, presents conclusive evidence that anoxia in the pregnant mouse is capable of producing congenital malformations of the eye of the offspring. Among these changes are those affecting the retina, such as retinal folding, coloboma and eversion of the retina, absence of the anterior chamber, and proliferation of vasoformative tissue.

They point out that similar defects in the offspring arise as well from other forms of trauma to the pregnant mother, such as radiation with X rays, metabolic injuries, or vitamin-deficient diets.

From their study of experimental teratol-

ogy, they conclude that "unrelated agents acting during pregnancy may give rise to the same type of disorder and that the resulting anomaly is expectedly a function of the stage of development at which the agent is active."

Yet the fact that, by experimentally subjecting the pregnant mouse to anoxia, they have succeeded in producing in the offspring defects of the retina, particularly the proliferation of vasoformative tissue, supports Szewczyk's thesis most aptly.

On the other hand, the third paper by Hugh Ryan, supporting the work of Kate Campbell (M. J. Australia, 11:2, 48, 1951), advances the idea that retrolental fibroplasia is due to the toxic effect of oxygen and that this disease develops as the result of "the stimulation of mitoses and overgrowth of connective tissue, increase of vascularity, and increased growth rate of the inner layer of the optic cup leading to further detachment," by excessive oxygen treatment. The evidence for this theory that Ryan presents is not so substantial as that given by the other authors, yet there is enough of it to cast some doubt which will need to be resolved by future carefully controlled studies.

The disease entity known as retrolental fibroplasia is firmly established since Theodore L. Terry first drew attention to it in 1942. We know now that it is definitely a disease of prematurity, predominantly in infants whose birth weight is three pounds or less and of the gestational age of six to seven months.

It is primarily a disease of the retina and vitreous, coming on four to six weeks after birth, at which time dilatation of the retinal vessels is first observed, followed by retinal and vitreous hemorrhages, exudate, retinal separation, neovascularization, and a cyclitic membrane leading to fibrous organization of fused retina behind the lens.

The incidence varies greatly in different parts of this country and the world but is apparently rising. The etiologic agent is entirely unknown, although much speculation on this score has arisen, and optimistic reports have been published, only to be discarded with disappointing time. No effective therapeutic agent is known, and experience with ACTH and cortisone, at first promising, has probably now been shown to be ineffective and quite dangerous to life.

There are three clinical stages of the disease (Owens and Owens):

Stage I. The stage of change in the retinal vessels (marked dilatation of the veins and tortuosity of the arteries).

Stage II. Involvement of the retina (clouding or graying of the retina, usually in the periphery near the ora serrata, and eventually leading to separation and scattered retinal hemorrhages).

Stage III. Involvement of the vitreous, cyclitic membrane formation, and fibrous tissue development.

Pathologically, however, the earliest lesions so far observed microscopically by W. C. Owens and Jonas Friedenwald (Tr. Am. Ophth. Soc., 1951, in press) is found in the nerve-fiber layer of the retina.

Here are seen patches or areas of proliferating endothelium, surrounded by an increase in the number of glial cells. Then areas of edema and small hemorrhages in the retina are observed. The next change is that of a rupture of the internal limiting membrane with proliferation of the endothelial cells into budding new vessels along the inner layer of the retina and into the vitreous. Eventually, this tissue, increasing in density and quantity, becomes part of the loops of the elevated retina which coalesce to form the fibrous disorganized mass of tissue of the end-stage.

It is known that Stage I and early Stage II are capable of spontaneous reversal. W. C. Owens mentions that "approximately 60 percent of the cases showing early manifestation of the disease will show no serious residual in the form of partial or complete retrolental membranes without any type of treatment." That is why the evaluation of effective treatment is so difficult. Stage II

(late) and Stage III are irreversible.

So much and no more do we know. Everything else is purely speculative, yet we have come a long way in the last 10 years in the understanding of this affliction so terrible to our new-born infants and so shattering to the young parents of every economic group.

The theory of anoxia as the etiologic factor is most appealing and, in spite of Ryan and Campbell, quite logical. C. J. Rudolph (J. Indiana State M. A., **44**:1161, 1951), in discussing retrolental fibroplasia and anoxia, enumerates some factors that predispose to an anoxia in the premature infant, as follows:

"1. Premature disruption of the maternal circulation from any cause.

"2. Inability of the fetal circulatory system to carry on normally its physiologic functions because of immature development.

"3. Anemia of prematurity which is more severe than in full-term infants.

"4. Incomplete saturation of existing hemoglobin from immaturely developed lungs and respiratory controls.

"5. Anoxia due to pressure on the soft, malleable head against the pelvic floor during the second stage of labor.

"6. Anoxia of the premature due to oversedation and deep anesthesia.

"7. Knee-chest position of babies sleeping on their faces on the mattress.

"8. Frequency of the disease in premature twins where maternal circulation is divided between two fetuses.

"9. Bilateral involvement, suggesting a systemic rather than a local involvement of the eyes only.

"10. Vaginal bleeding in 30 to 35 percent of mothers giving birth to children developing retrolental fibroplasia (Reese).

"11. Bassinets do not encourage the circulation of air.

"12. Warm temperatures in the nurseries accelerate the body metabolism and, even though the oxygen ratio of the environmental air be increased, this may not be sufficient to meet the requirements.

"13. No tissues in the body require as much oxygen as do the nervous system and retina.

"14. With anoxia there is a measurable increase in the size of the vessels, varying between 10 and 20 percent, which is more marked in the veins (R. A. McFarland, et al.: Arch. Ophth., **26**:886, 1941)."

These are potent arguments to which could be added the frequency of the presence of severe upper respiratory infections in some of the affected prematures.

T. H. Ingalls in a most illuminating paper, "The study of congenital anomalies by the epidemiologic method" (New England J. Med., **243**:67, 1950), points out that congenital malformations are now known to be either inherited or acquired during pregnancy as the result of maternal disease, and, like other disease, prenatal conditions may be explored through case study, group study (epidemiology), and experimentation.

Anoxia is postulated as an important cause of maldevelopments such as mongolism, cyclopean or anencephalic monsters, and others. Among his conclusions, Ingalls says "retrolental fibroplasia is interpreted as a stage-specific ocular defect of the prematurely born fetus. The problem, which is of epidemiologic as well as ophthalmologic, pediatric, and obstetric concern, should be attacked simultaneously by coöperating groups of workers. It is as ripe for solution as congenital cataract was in 1940."

The solution of this puzzle seems indeed to be ripening and there is cause for optimism both in the prevention and early treatment of this dread condition.

Derrick Vail.

OBITUARY

WALTER BRACKETT LANCASTER, M.D.
1863-1951

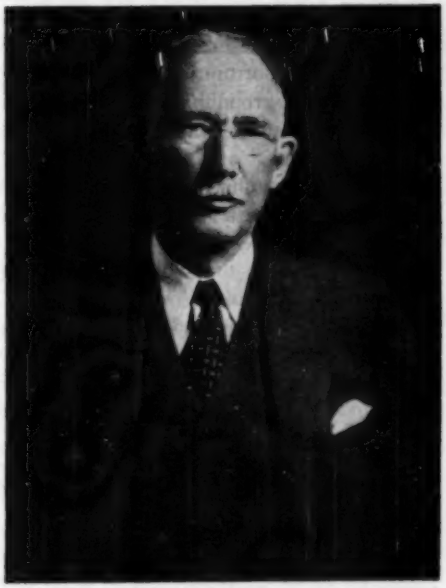
One of the best known figures of American ophthalmology passed from the scene when Walter Brackett Lancaster died suddenly in Boston on December 9, 1951.

He was born on May 11, 1863, at Newton, Massachusetts, the son of Charles Bartlett Lancaster and Mary Elizabeth Brackett. Both his father and mother traced their ancestry back to the Mayflower pilgrims. He graduated from Harvard College *magna cum laude* in 1884, and from Harvard Medical School in 1889. After several years' study in European clinics, he returned to Boston to begin general practice, but shortly thereafter devoted himself entirely to ophthalmology.

He joined the staff of the Massachusetts Eye and Ear Infirmary in 1897 and rose to the rank of surgeon in 1920. Except for a period of enforced absence due to poor health, he maintained his connection with that institution until his death. He resigned from the active staff in 1926 because of the pressure of private practice, but thereafter remained as consultant. He was also ophthalmic surgeon at the Boston City Hospital for a number of years.

His university connections included the Harvard Medical School, in which he gave postgraduate courses for over 40 years, and the Dartmouth Eye Institute to which he was called as chief-of-staff in 1939. After serving in this capacity for two years, he resigned and returned to private practice in Boston.

Dr. Lancaster was interested in many phases of ophthalmology and his contributions to the literature were varied. In reviewing his bibliography, one finds his chief interest appears to have been in problems of illumination, physiologic optics, refraction, disturbances of ocular motility, aniseikonia, and orthoptics. He also wrote papers on surgery, chiefly of the extraocular muscles. One of his most important contributions was his work on the standard nomenclature of ocular disease and the proper terminology in ocular motility. Just before his death, he completed a book on refraction and motility, which will be published shortly.



Walter Brackett Lancaster

He was a regular attendant at meetings and took an active part in discussion of the papers. These discussions were characterized by fairness in dealing with conclusions he did not agree with and by a simplicity of expression in bringing out the main points of any paper.

One of Dr. Lancaster's primary interests was in postgraduate education. Early in his career he began giving courses on physiologic optics at Harvard Medical School. He was one of the original members of the American Board of Ophthalmology, which was founded in 1916, the first certifying specialty board in the country. He served on this board for many years and, after his

term of office finally came to a close, he continued as a consultant up to the time of his death.

At the conclusion of World War II he foresaw the great need for providing a course in the basic sciences for those medical officers returning from the Armed Forces who could not be accommodated in the regular university courses. Along with Dr. Judd Beach and Dr. Theodore Terry, he formed the Ophthalmological Study Council which has functioned ever since with signal success in providing opportunities to many young doctors to get a grounding in basic ophthalmology. This course is now known as "The Lancaster Course" and stands as a fitting tribute to the ingenuity of a man who, at the age of 83 years, saw a great educational need and took steps to remedy it.

Not content with this, he then started, in 1948, a summer course for orthoptic technicians wherein a number of young women received didactic training in Boston for 10 weeks and were then assigned to various offices and clinics throughout the country for practical work.

Most of his life he was embarrassed by poor health. He graduated from medical school two years late because of it. In 1901, he had to retire from practice for about nine years, until finally the removal of a chronic adherent appendix improved him. During the last 10 years of his life he was a sufferer from angina which necessitated the use of nitroglycerin tablets at frequent intervals. And yet he carried on right up to the end, never complaining, and often joking about his infirmities.

Most of the honors that ophthalmology has to offer were conferred on him during his lifetime. He was a member of all the best known societies, being elected chairman of the A.M.A. Section, president of the American Ophthalmological Society, and of the American Academy of Ophthalmology and Otolaryngology. In 1939 he received an honory degree of Doctor of Science from Dartmouth. He was the recipient of the Howe Medal in 1941 and the Dana Medal in 1943. In May, 1943, the AMERICAN JOURNAL OF OPHTHALMOLOGY published the Lancaster Testimonial issue, comprising a number of contributions by former students and colleagues.

Walter Lancaster's life spanned an important part of American history. At his birth, Grant was besieging Vicksburg. When he died, the Korean episode of the struggle against world communism had become a stalemate. Between came two world wars, in one of which he served with distinction.

In the field of ophthalmology he witnessed stupendous changes. The year he entered medical school, Koller demonstrated the practical value of cocaine as a corneal analgesic. The following year von Hipple performed the first successful corneal graft in animal eyes. Shortly thereafter Credé introduced his silver-nitrate prophylaxis for gonorrheal ophthalmia of the newborn.

Other important developments included new concepts in ocular pathology, physiology, and surgery, the use of miotics in the treatment of glaucoma, X-ray localization of intraocular foreign bodies, instrumental tonometry, biomicroscopy of the living eye, fundus photography, the antibiotics in the control disease, and finally the discovery of cortisone and corticotropin.

It was a long life and an interesting one. Walter Lancaster absorbed much wisdom and developed a calm philosophy which was to stand him in good stead in times of illness and sorrow. His influence as an educator was great. He will be sorely missed by a host of devoted colleagues.

Edwin B. Dunphy.

WALTER B. LANCASTER, M.D.

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CORRESPONDENCE

RETROLENTAL FIBROPLASIA

Editor,
American Journal of Ophthalmology:

I am writing in regard to the first article in the December, 1951, AMERICAN JOURNAL of OPHTHALMOLOGY on retrolental fibroplasia.

When we are dealing with an unknown quantity our minds should be kept open. Often positive statements may prevent real solution. The first statement in the above-mentioned article is a direct statement without qualification, that discovery has been made that retrolental fibroplasia was directly related to oxygen environment.

We have an excellent premature station here at Children's Hospital in Chattanooga, Tenn. We have complete Isolet service with oxygen for all babies. Oxygen is used continuously until the child is ready to go to the graduate nursery for discharge (weight five pounds). Many of our babies stay in oxygen for 60 to 90 days.

In spite of this we have had eight cases of retrolental fibroplasia this past year.

The eyeground checks have not been universal but those made have failed to show any eyeground changes up to the time of discharge either in or out of oxygen.

I am writing this not to raise an issue, but to voice a note of caution. Observations must be carried on in larger series, and must be confirmed by other investigators before final conclusions can be drawn.

We must remember that writings accepted by the JOURNAL carry weight with those who read them.

(Signed) H. D. Long,
Chattanooga, Tennessee.

STANDARDIZATION OF TERMINOLOGY

Editor,
American Journal of Ophthalmology:

I should like to call the attention of your contributors and readers to an inconsistency in ophthalmological orthography and to plead for a standardization of terminology.

Phacoerysis, the technique known also as Barraquer's method after the originator of the procedure in cataract surgery, appears in English in four forms among the 79 references listed in the *Index Catalogue* of the Surgeon General's Office (facoerisis, phacoerisis, phacoërisis, phakoerisis[1]); in three forms in two standard medical dictionaries (phacoerysis[2] phacoerisis, and phakoerisis[3]); in two forms in an index of the AMERICAN JOURNAL OF OPHTHALMOLOGY (phacoëresis and phacoërisis[4]); and in additional form in periodical literature (facoeresis[5]).

The name of the instrument entertains the same pattern of variation: erysiphake,[6] erisophake,[7] erisifaco,[8] erisiphaque,[9] erisiphake,[10] eresiphake,[11] and erisophac.[12]

In his original article Barraquer gave the derivation of the instrument as Greek, from ἔρυσις, a drawing (or sucking) out, and φακός, lentil (whence lens), and of the operation from the same words in inverted order.[13]

Following customary American transcription of Greek, the words should properly appear in our texts as phacoerysis and

erysiphake respectively. Although purist preference nominates these spellings, recent usage seems to favor phacoerisis and erisophake. In any event, the present system of numerous variants for a 35-year-old procedure should be abandoned and uniform spelling should be adopted.

(Signed) (Mrs.) Thelma Charen,
Subject Header, *Current List of Medical Literature*, Army Medical Library, Washington, D.C.

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BOOK REVIEWS

TUMORS OF THE EYE. By Algernon B. Reese. New York, Paul B. Hoeber, Inc., 1951. Cloth binding, 560 pages, 511 illustrations, 122 in full color, bibliographies, index. Price: $20.00.

"It is better not to treat anyone afflicted with occult cancers, for if one treats them, they rapidly die; if one does not treat them, life is prolonged."

Hippocrates, *Aphorisms*, 16:38
(Littre, 4:573, 1844.)

This is one of the most important books on a special subject in ophthalmology that has appeared in more than several decades. The years of experience of its author in the clinic and in the pathologic laboratory, the meticulous care of his study reflected on every page, his scientific integrity, and his lucid style assure an accuracy of text that will be difficult to equal and impossible to surpass. His choice of beautiful and clear illustrations has been exceedingly apt, and their reproduction is the highest achievement of the bookmaker's art. We are most grateful to author and publisher for this superb tool.

Although ophthalmic literature has been extraordinarily rich in articles on neoplasms of the eye and orbit, there have been very few books devoted to this important subject. In 1868, our own Hermann Knapp published a book on "Die Intraocularen Geschwülste" (Karlsruhe) which created wide interest. In 1886, the Portuguese, da Gama Pinto, published a monograph, "Über Intraocularen Tümoren" (Wiesbaden).

An important step forward was the appearance in 1901 and 1904 of the first scientific work, Pierre Lagrange's "Traité des Tumeurs de l'Oeil" (Paris) in two volumes. In 1926, Victor Morax issued his "Cancer de l'Appareil Visuel" (G. Doin), a volume of 495 pages and four color plates of photographs beautifully reproduced. Morax's contribution included not only his own important observations but a complete review of the literature since the publication of Lagrange's work. Twenty-five years later

appears Reese's book and, about the same time, Guy Offret's work of 542 pages, "Les Tumeurs Primitives de l'Orbite" (Masson) which will be reviewed later in these pages.

Dr. Reese, who is clinical professor of ophthalmology, College of Physicians and Surgeons, Columbia University; attending ophthalmologist and pathologist, Institute of Ophthalmology, Presbyterian Hospital, New York; and ophthalmologist to the Memorial Center for Cancer and Allied Diseases, New York, received the Howe Medal of the American Ophthalmological Society in 1950. The citation read in part "your continued interest and investigations in pathological lesions of the eye have enriched the knowledge of ophthalmology."

In the years of his professional life, Dr. Reese has been especially interested in ocular tumors, and his 22 years of close association with the great Memorial Center for Cancer and Allied Diseases, New York, have assured him of an extraordinary wealth of material for clinical and pathologic studies. Thus he is particularly well endowed for the gathering and presentation of the harvest of these years of endeavor.

There are 17 chapters in his book. They cover the subjects of epithelial tumors of the lids, conjunctiva, cornea, and uvea; retinoblastoma; glioma; meningioma; tumors of the peripheral nerves; pigmented tumors; angiomatous tumors; leiomyoma; tumors of connective-tissue origin; of bone and lymph tissue; mixed tumors; glandular tumors, dermoid cysts, metastatic tumors, and neoplasms of the orbit. Nothing is omitted.

Each chapter includes Dr. Reese's own accurate observations as well as those of other significant authors and clearly describes the diagnosis and, in proper detail, the steps in the treatment that are most suitable and satisfactory. The descriptions of surgery reflect Dr. Reese's fine skill and judgment.

The chapters on "Retinoblastoma" and on "Pigmented tumors" are particularly noteworthy for they include the subjects of the greatest interests of the author and in which he has made his most original and important contributions. His technique of radiation treatment of retinoblastoma and an analysis of the results obtained thereby are adequately described. The discussion of pigmented tumors is a most satisfactory guide to the clinician in charting his course through a treacherous sea.

Paul B. Hoeber, Inc., the medical book department of Harper and Brothers, New York, in publishing this work has used a fine quality of enameled paper that superbly brings out the details of the illustrations. The print is sharp and clear and recalls the beautiful pages of Berliner's *Biomicroscopy of the Eye* for which these publishers received a first prize (publishers') in 1943.

One can no longer subscribe to the aphorism of Hippocrates quoted as an introduction to this review.

Derrick Vail.

PHASE MICROSCOPY: PRINCIPALS AND APPLICATIONS. By Alva H. Bennett, Harold Osterberg, Helen Jupnik, and Oscar W. Richards. New York, John Wiley & Sons, Inc., 1951. 320 pages, profusely illustrated, bibliography, and index. Price: $7.50.

In the now familiar coated lens the reflected rays from the magnesium floride film and from the lens surface nullify each other and so abolish surface reflections. Phase microscopy on the other hand aims to promote contrast so that details of a transparent specimen may be observable which are almost invisible in the ordinary microscope. The essential elements are a phase or diffraction plate in the objective and a specialized condenser diaphragm.

If the latter is a clear annular opening, an annular ring corresponding to its image is left uncoated in the phase plate. All the direct light must pass through this ring; other light diffracted by the structure of the specimen passes through the remainder of the phase plate, which thus can introduce

phase and intensity differences between the specimen and its surround.

Phase differences are created by evaporating on a plane glass plate a dielectric material like magnesium fluoride to the required thickness; absorption is introduced by subsequent deposit of a metallic film, usually Inconel. In this process the application of masks assures the pattern required.

With present-day phase microscopes, a specimen can be rendered visible when the optical path difference between it and its surround is well below a 1:100 wave length. The phase microscope renders possible also a fairly precise determination of the refractive index of the specimen provided its surround approximates the same index. Ajo, in 1947, reported the findings by this method of the refractive index of the retina.

With the phase microscope, the vitreous is seen composed of fibers, cells, and media of different optical densities. Studies on the fresh cornea show that a mounting isosmotic for the epithelium is not correct for the stroma. The corneal tissue soon degenerates under observation and then reveals nerve cells and fibers.

The utilization of phase differences in microscopy, a dream of Abbe's, was realized by Zernike in 1935, and a suitable instrument was produced by the Zeiss works in 1941. In the decade since, the authors, all from the staff of the Research Laboratory, American Optical Company, have elaborated with typical American vigor the possibilities of phase microscopy; produced a range of diffraction plates suitable for all types of specimens; and have had their refinements incorporated in the American instruments.

Phase microscopy is here to stay and the present text, which covers every phase of the subject, is worthy of the definitive place of this method in clinical study and modern research.

James E. Lebensohn.

SPECIFIC DYSLEXIA (Congenital Word-Blindness). By Bertil Hallgren. (Translated into English by Erica Odelberg.) Copenhagen, Ejnar Munksgaard, 1950. Price: Not listed.

The danger of accepting or implying that dyslexia is hereditary without proper evidence should be challenged, and it is mainly about the author's conclusions on this point that this review centers. In order to get a careful review from several different approaches, I asked Dr. Beverly Cox, psychologist, Dyslexia Memorial Institute at Northwestern University, Dr. A. R. Gilliland, professor of psychology, Northwestern University, Prof. Alfred Schmieding, dean, Concordia Teachers College, and Dr. Frank M. Lorimer, psychiatrist, Dyslexia Memorial Institute, to collaborate.

Hallgren's monograph is a careful statistical and theoretical study of 276 cases of "specific dyslexia." Including the siblings and parents, a total of 706 persons were incorporated in the investigation.

In addition to the 276 cases, the author reviews carefully over 200 studies of dyslexia and related problems, which makes the monograph an excellent source of reference material.

In general, the findings of the study are quite similar to those found by other investigators. Hallgren's conclusions, however, are not. One gains the impression that Hallgren had a preconceived idea and has attempted to prove it. To illustrate his logic, I quote: "The *fact* that specific dyslexia can be shown to be hereditary in the overwhelming majority of families in which the patient has some nervous disorder is a strong argument a posteriori against the hypothesis that specific dyslexia is secondary to the nervous disorders in these cases."

Discussing physical illnesses, Hallgren states; "I consider that such illnesses only affect the child's reading ability that would cause him to be away from school during the first two years." This could hardly be considered adequate criteria for physical ill-

nesses, for in our experiences we have seen great influences in such ailments as glandular imbalances and malnutrition, which would not necessarily mean that the child would miss school.

With reference to cerebral disorders the author has held to a rather fixed neurologic type of examination. In ruling out emotional disturbances as being of importance, he assumes, in his conclusions, that the incidence of emotional disturbances in children with reading problems is no higher than in the normal population, yet Hallgren admits, and his statistics demonstrate, that in his cases, emotional disturbances were extremely common.

Some of the literature dealing with association between reading difficulties and visual defects is discussed. Among other conditions, Hallgren calls attention to the fact that compensated muscle imbalances, such as phorias of high degree, do not affect interpretation of symbols but that effort to see binocularly can be said to discourage reading. It appears that he considers ocular disturbances of little essential importance in dyslexia. He states that in none of the cases in which glasses were prescribed had there been subsequently noted any marked improvement in reading and writing. He apparently failed to consider abnormalities of the eyes as only part of the symptom complex in retarded reading.

Because the author found that, in 80 percent of his cases of dyslexia, one of the parents was also dyslexic, he concludes that heredity was the causal factor. On the surface this appears to be a valid reason for saying that hereditary factors are of paramount importance in reading disability. Certainly the author has proved that reading difficulties tend to run in families, but it seems pertinent to question whether the trait runs in the family because it is inherited or because the same environmental factors also tend to run in families.

Although Hallgren's basic theory of genetically transmitted specific dyslexia is not accepted, there is nevertheless a possibility that heredity may occasionally contribute circumstances that predispose to dyslexia; and his thorough and painstaking study is, therefore, appreciated. Acceptance of the hereditary concept would be disastrous, for then the parents, teachers, and particularly the child would consider the condition hopeless and treatment would be doomed to failure.

The causal factors may be central or peripheral, or both, and under abnormal environmental and functional changes appear as a syndrome, with many ramifications extending into the emotions, health, and education of the child. This syndrome—dyslexia—is characterized by an inability to learn to read properly, even though the individual may have normal or superior intelligence.

In all of these perplexing problems, with few exceptions, it can, fortunately, be demonstrated that dyslexia does yield to treatment, but successful treatment takes the best that medicine, psychiatry, psychology, and education have to offer.

George E. Park.

CANCER AS I SEE IT. By Henry W. Abelmann, M.D. New York, Philosophical Library, 1951. 95 pages and index. Price: $2.75.

Carcinoma, sarcoma, pernicious anemia, leukemia, Paget's disease, rodent ulcer, Hodgkin's disease, mycosis fungoides, and certain granulomas are all linked together in the mind of the author as manifestations of cancer and are believed by him to be caused by a mold fungus. The book is a philosophical discussion, without sufficient factual or experimental evidence to lend credence to the hypothesis presented.

William A. Mann.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Ogle, K. N. **Optics and visual physiology. Review of literature for 1949 and 1950.** A.M.A. Arch. Ophth. **45**:684-703, June, 1951.

This is a detailed review of the current literature on the subject. John C. Long.

Parnell, R. W. **Sight of undergraduates. Loss of visual acuity.** Brit. J. Ophth. **35**: 467-472, Aug., 1951.

Parnell states that 31 percent of undergraduates wear glasses and that the sight of students is about four times poorer than that of a similar age group in the general population. The vision of college students deteriorates during their four years at the university. Students with the lowest visual acuity tended to have the most marked decrease in vision and the better students to have poorer sight. (4 tables) Orwn H. Ellis.

Pascal, J. I. **Power of the lacrimal layer in the corneal contact lens.** A.M.A. Arch. Ophth. **45**:194, Feb., 1951.

The corneal contact lens is applied to the eye without a solution, and there is only a capillary layer of tears between the lens and the cornea. Previous calculations of the power of this lacrimal layer have been in error. The author gives his calculations, and shows the power of this layer to be approximately −13.00 D.

John C. Long.

Posner, A., and Schlossman, A. **Relation of diplopia to binocular vision in concomitant strabismus.** A.M.A. Arch. Ophth. **45**:615-622, June, 1951.

Diplopia in strabismus can be explained on principles derived from normal physiology. Ocular dominance determines the fixing eye and also the degree and extent of suppression. If conditions are so altered by surgical correction that the images fall on areas of the retina which have not developed the ability to suppress, diplopia results. Since the elements of binocular vision can be traced to the more general neurologic and psychologic phenomena which are associated with the gestalt concept, binocular vision may be interpreted as a special application of the gestalt concept. John C. Long.

Sato, T. **Summary of my various experiments upon myopia (especially upon the cause of near work myopia).** Yokohama Med. Bull. **2**:41-67, 1951.

The author examined 1,034 children under atropine and found a diminution in emmetropia and low myopia, an increase in hypermetropia, and no change in high myopia. The low, or school, myopias may be considered due to the tonus of the ciliary muscle, with a refractive lenticular change. As the process continues, an organic change ensues. The author recommends a reduction in the amount of near work in school children, adequate use of spectacles, slight undercorrection of refractive errors, the use of convex lenses, and the use of atropine as a cycloplegic.

Irwin E. Gaynon.

Sloan, L. L. **Measurement of visual acuity.** A.M.A. Arch. Ophth. **45**:704-725, June, 1951.

The familiar nonserif letters selected to be approximately equal in legibility are still the best available type of test target for literate subjects. Measurement of acuity for screening and classification should be made at a distance of about 6 meters with a brightness of 12 to 18 millilamberts. The visual acuity of each eye should be determined with occlusion of the other eye. There is room for further investigation. (9 figures)

John C. Long.

5

DIAGNOSIS AND THERAPY

Anderson, O. E. E. **Theoretical considerations for an artificial corneal implant.** Brit. J. Ophth. **35**:628-630, Oct., 1951.

A glass disc, 4 mm. in diameter, is sealed inside a tantalum ring. At operation, a 4 mm.-disc is cut from the cornea and the remaining corneal rim split to allow the insertion of the tantalum flange. The implantation of inert transparent discs in opague corneas has been attempted repeatedly with greatly limited success, the first nearly a century ago, but the demonstrated tolerance of tantalum by the ocular tissues and the glass-to-metal sealing common in the electronics industry offer a new approach. (2 figures)

Orwyn H. Ellis.

de Conciliis, Nicola. **The use of the mobile ocular prosthesis of Stone-Jardon.** Arch. di ottal. **54**:177-188, Sept.-Dec., 1950.

The Stone lateral-edge implant is described and the technique of its application is illustrated by 8 figures.

John J. Stern.

Cüppers, C. **A new method for the continuous registration of the consensual pupillary reaction.** Klin. Monatsbl. f. Augenh. **119**:411-417, 1951.

This new instrument for pupillographic studies continuously registers the movements of the iris and was designed to study the correlation between photochemical processes in the retina and the pupillary movements. Ernst Schmerl.

Egan, J. A. **A modified cross cylinder.** A.M.A. Arch. Ophth. **46**:153-154, Aug., 1951.

By shifting the position of the handle of the Jackson cross cylinder it becomes possible to use the instrument in a less awkward manner when determining the axis in oblique positions. John C. Long.

Falls, H. F., Bassett, R. C., and Lamberts, A. E. **Ocular complications encountered in intracranial arteriography.** A.M.A. Arch. Ophth. **45**:623-626, June, 1951.

Eighty consecutive cases of intracranial angiography have been reviewed for evidence of ocular complications. The radiopaque material, thorotrast or iodopyracet, was injected into the common carotid artery. Petechial hemorrhages of the skin of the eyelids, of the palpebral and bulbar conjunctiva and of the retina were demonstrated. Pupillary dilatation,

optic neuritis, angiospasm of the retinal vessels and blindness were also encountered. The cause of these complications is not known, but they undoubtedly result from vascular changes secondary to allergic, toxic or physical phenomena.

John C. Long.

García Nocito, P. F. **Ocular diseases and cortisone.** Semana méd. **99**:531-536, Sept. 20, 1951.

The author describes local treatment with ACTH and cortisone (instillation, ointment, subconjunctival and retrobulbar injection) and summarizes his experience. Good results are obtained in the treatment of chemosis and corneal vascularization after burns, in vernal catarrh, allergic conjunctivitis, atropine irritation and especially in phlyctenular keratoconjunctivitis. The drug has been beneficial in cases of oculofacial pemphigus. In corneal diseases, the early good results in marginal ulcers are often followed by relapse when treatment is stopped; in rosacea keratitis it is beneficial, but doubtful results are obtained in superficial keratitis, luetic parenchymatous keratitis and opacified grafts. In non-specific interstitial keratitis results are better. Excellent results have been obtained in anterior uveitis, and improvement in postoperative iridocyclitis, and several workers have reported excellent results in retrolental fibroplasia. Cortisone may be a useful adjuvant in the treatment of choroiditis. In glaucoma only cases secondary to hypertensive iritis have shown good results. In retinal and optic nerve diseases cortisone is not effective; in sympathetic ophthalmia reports of treatment are contradictory. In exophthalmos, apart from a case report by Coles, the results are poor. (48 references)

A. Arruga.

Gerspacher, T. S., Fowler, H. D., Jr., and Rolf, D. E. **New plastic surgical drapes.** A.M.A. Arch. Ophth. **45**:673-677, June, 1951.

Plastic eye drapes are made of an inert, nonabsorptive and nontoxic material. They are secured to the operative site by a pressure-sensitive adhesive substance which eliminates the need for pins and towel clips. The drapes are packaged sterile and will maintain their sterility indefinitely. They are prepared in four sizes for use in different operative sites.

John C. Long.

Ingman, W. **Portable test-type.** Brit. J. Ophth. **35**:631, Oct., 1951.

The portable test-type apparatus consists of a collapsible tripod to which the chart and a spot light are attached. An added strip-light gives further illumination. The apparatus can be carried in a small bag. Orwyn H. Ellis.

Johnson, L. V. **Conversion adapter.** A.M.A. Arch. Ophth. **45**:195, Feb., 1951.

This adapter converts the focal length of the light beam of the Poser slitlamp from 75 mm. to 100 mm., and makes it possible to examine the lens and anterior vitreous with greater accuracy.

John C. Long.

King, J. H., Jr., and Forrest, R. L. **A modified strabismus muscle forceps.** A.M.A. Arch. Ophth. **46**:155-156, Aug., 1951.

The Jameson and Prince recession forceps has been modified to provide a lower lip which protrudes 1 mm. from the instrument. A groove is ground in this lip. The tendon is severed with a sharp knife cutting against the groove in the protruding lip. In this way a clean, even muscle stump is obtained with no danger of injury to the sclera. John C. Long.

Krimsky, Emanuel. **A combination square prism and lollipop holder.** A.M.A. Arch. Ophth. **46**:337-338, Sept., 1951.

In order that the patient or the examiner can hold a square prism more easily and accurately, the author has attached a short rod. The combination apparently suggests a lollipop to those who are familiar with this juvenile confection.

R. W. Danielson.

Krimsky, Emanuel. **An illuminated monocular eyeglass loupe.** A.M.A. Arch. Ophth. **46**:339-340, Sept., 1951.

A light, easily handled, illuminated monocular eyeglass loupe is described and illustrated. It is combined with a small illuminating system and can be made to fit firmly on any size or shape of spectacle frame.

R. W. Danielson.

Lister, A. **Appliances: a small gonioscopy lens.** Brit. J. Ophth. **35**:505-506, Aug., 1951.

The lens for inspecting the filtration angles and for carrying out goniotomy under direct view is small and easily handled, and can be used with or without a speculum. It rests directly on the cornea and air collecting beneath is displaced with a lacrimal syringe.

Orwyn H. Ellis.

Markham, Margaret. **Modifications of the Zeiss-Nordenson retinal camera.** A.M.A. Arch. Ophth. **46**:148-152, Aug., 1951.

The use of a Bantam back as a film holder permits the use of eight exposure rolls of color film. An adjustment must then be made in the focus. A modification of the cable-release mechanism and conversion of the stereoscopic model into a monocular instrument are described.

John C. Long.

Neubert, F. R. **Case notes: Observations on the sugar content of the cerebrospinal fluid. Foster Kennedy's syndrome.** Brit. J. Ophth. **35**:621-622, Oct., 1951.

In the case of Foster Kennedy's syndrome reported, the cerebrospinal fluid was found to be sterile in repeated examinations but there was a reduction in sugar content. Streptomycin and chloromycetin had been given, and both contain a glucose reducing substance. These data are reported to call attention to the fact that the sugar content of the cerebrospinal fluid cannot be used in differential diagnosis when these drugs are used.

Orwyn H. Ellis.

Putnam, O. A., and Quereau, J. V. **The tropophorometer.** A.M.A. Arch. Ophth. **45**:186-193, Feb., 1951.

A tropophorometer is described in which a new system of coordinates is employed. This eliminates the necessity for a correction factor in vertical readings. The advantages of this new system of coordinates recommends its use in instruments for the more accurate measurements of heterophoria and heterotropia.

John C. Long.

Ruben, C. M. **Portable perimeter.** Brit. J. Ophth. **35**:634-635, Oct., 1951.

A transparent portable hemispherical perimeter is described. The normal field outlines are marked on the dome's surface. Any of the regular test targets may be used. The instrument is mounted on a telescopic stand and is light and portable.

Orwyn H. Ellis.

Sanna, M. **The graticule test (Amsler) for examination of the macular function.** Boll. d'ocul. **30**:489-498, Aug., 1951.

Amsler described the graticule test for macular function (Ophthalmologica, 1947) in which a white network of 400 little

squares on a dull background and covering, at proper exposure, a square of the retinal surface 20 degrees in length and width. A single little square covers an area of just one degree. Three patients with a normal fundus were examined by this method and showed definite scotomas; in five other eyes, regression of the scotoma could be demonstrated with the graticule when the ophthalmoscopic picture was still unaltered. K. W. Ascher.

Shurr, P. H. **Angiography of the normal ophthalmic artery and choroidal plexus of the eye.** Brit. J. Ophth. **35**:473-478, Aug., 1951.

In serial films of angiographic studies, the ophthalmic artery was visible, and could be followed in detail. The choroidal plexus appeared as a thin crescent in many of the films and seemed to be filled during the venous phase of the examination. The orbital vessels were more clearly seen when an obstruction of part of the cerebral circulation was present. Diodone in the ocular circulation caused an intense burning and its use may not be without danger. Orwyn H. Ellis.

Trevor-Roper, P. D. **Present status of physiotherapy in ocular disease.** Brit. J. Ophth. **35**:583-594, Oct., 1951.

The author evaluates the status of each of the methods of physiotherapy used in ophthalmology. Treatment with generalized ultraviolet light has been of doubtful value and local application has little if any advantage over other forms of treatment. Infrared radiation has little application in ophthalmology and ultra-sonic therapy has been used very little. The principal objection to the latter is that it may cause concussion cataract. In electrotherapy, electrolysis, galvanism and faradism have been used with some success, but about half of the cases treated were not improved. When treated with diathermy there was relief from pain, but it was questionable that improvement was any faster than with other method. In general, except diathermy, all physiotherapy is of questionable value in ocular disease. Orwyn H. Ellis.

van der Tweel, L. H., and Bleeker, G. M. **Recording pupillograph of simple design. Preliminary report.** Brit. J. Ophth. **35**:632-633, Oct., 1951.

The eye is focused on a film which is rotated slowly in a vertical direction. A horizontal slit is fixed near the film where the middle of the pupil is projected. Blue-sensitive film is used for blue and gray eyes, and red-sensitive film for dark-brown eyes. Pupillograms are recorded.
Orwyn H. Ellis.

Young, J. H. **A new ocular prosthetic aid: the intra-ocular implant.** Brit. J. Ophth. **35**:623-627, Oct., 1951.

A plastic implant to be used in an eviscerated globe is described. So that healing takes place in proper position, the implant is fixed with tantalum wires which pass through the sclera. A peg on the anterior surface at operation is passed through a hole in the cornea. This peg acts as an obturator on which the prosthesis rests. After evisceration of the global contents, the tantalum wires are passed through the sclera and through the holes drilled in the implant, and the peg projects through a hole made in the cornea. The scleral wound is closed and the entire contents are covered with the conjunctival and episcleral tissues. The wound is closed with interrupted black-silk sutures. Daily dressings are advised. After about 10 days the peg of the implant protrudes through the wound. An advantage of this procedure is excellent mobility. Orwyn H. Ellis.

6

OCULAR MOTILITY

Brockhurst, R. J., and Lion, K. S. **Analysis of ocular movements by means of an electrical method.** A.M.A. Arch. Ophth. **46**:311-314, Sept., 1951.

A recording of the varying electrical potentials, picked up by means of electrodes placed behind the external canthi of the subject, show the movement of the eyes.

R. W. Danielson.

Lion, K. S., and Brockhurst, R. J. **Study of ocular movements under stress.** A.M.A. Arch. Ophth. **46**:315-318, Sept., 1951.

The acceleration of the eyeball, which is proportional to the muscular force causing the eye movement, was measured with the authors' electronical method in subjects who were asked to fixate two alternately flashing lights, 90 degrees apart, at a rate of 120 to 150 changes per minute. No evidence of fatigue of the extrinsic ocular muscles was found. Instead, a decreased excursion of the eyes or an inability of the subject to move the eyes rhythmically and in step developed after a time. R. W. Danielson.

McGrath, Harry. **Alopecia associated with an intraocular foreign body.** A.M.A. Arch. Ophth. **46**:319-325, Sept., 1951.

The development of alopecia of the scalp, brows, and cilia was noted six weeks after removal of an intraocular foreign body. The changes in this patient seem to be manifestations of alopecia traumatica caused by cranial injury in a man of neurotic disposition. The occurrence of this change after unilateral traumatic uveitis may throw light on the origin of similar changes, in Vogt-Koyanagi disease, a bilateral nontraumatic idiopathic uveitis, and in sympathetic ophthalmia. R. W. Danielson.

Sarkies, J. W. R. **Case notes: ophthalmoplegia following a scorpion bite.** Brit. J. Ophth. **35**:502-504, Aug., 1951.

In a case of complete ophthalmoplegia after a scorpion bite, surgical treatment was used to correct the ptosis and the position of the globe with good cosmetic and functional results. The neurotoxic properties of the venom of scorpions resembles snake venom and caused a peripheral neuritis of the third cranial nerve.

Orwyn H. Ellis.

Sloane, Albert E. **Analysis of methods for measuring diplopia fields.** A.M.A. Arch. Ophth. **46**:277-310, Sept., 1951.

The author provides an extensive description of all of the important methods of clinical study of ocular motility. He exhibits the theoretical considerations upon which the tests are based and makes clear the value and the range and limits of the usefulness of each test. Those who understand this subject as well as Dr. Sloane does may not want to read the original. Most ophthalmologists will be grateful for this comprehensive exposition which will enable them to evaluate, and most probably greatly improve, their own procedure. The data cannot be presented in abstract because those who will use the information will hardly want less than the original description. R. W. Danielson.

Urist, Marlin J. **Horizontal squint with secondary vertical deviations.** A.M.A. Arch. Ophth. **46**:245-267, Sept., 1951.

Of 615 patients with horizontal squint, 79 percent were found to have a vertical component, and half of these had bilateral elevation or depression combined with esotropia or exotropia.

The vertical deviations are considered to be secondary to the horizontal squint, and the differentiation from vertical deviations due to paralysis of individual vertical muscles is important because in

these patients the horizontal squint must be corrected first. If the correction of the lateral squint is successful the vertical deviation will be much improved or will completely disappear. (4 tables, 12 figures) R. W. Danielson.

7

CONJUNCTIVA, CORNEA, SCLERA

de Andrade, Lopes. **Trachoma. Diagnosis and treatment.** Brit. J. Ophth. **35**: 601-606, Oct., 1951.

There is often a remarkably consistent lymphocytosis in trachoma which is of help in making a diagnosis. Granulations and pannus are most important and must be carefully examined and classified. Characteristic features in the history also aid in the differential diagnosis. In the early stages biopsy may be of little value, but as the disease progresses the histological changes are remarkably constant; there is a central epithelial zone and a peripheral lymphocytic zone and plasma cells, Leber's cells and vesicular cells are present. Many different types of treatment have been used. Neither aureomycin nor penicillin cured the disease but cleared secondary infection. The author includes silver nitrate, copper sulfate, and sulphonamides systemically, and surgical correction of the complications of the cicatricial stage in this treatment of trachoma. Cortisone is used to decrease the inflammatory reaction and combat secondary uveitis. Orwyn H. Ellis.

Beauvieux, J., Julien, R. G., and Chabot, J. **Pure florid trachoma treated by aureomycin.** Rev. intern. du trachome **28**:269-272, 1951.

A woman, 27 years old, showed bleb follicles and slight pannus, without any other infection complicating the trachoma. Treatment by aureomycin systemically in full dosage and by drops locally every two hours was continued for 16 days. The irritative symptoms subsided in four days, the follicles gradually disappeared and none were visible after five weeks. A slight pannus with fine neovascularization persisted. James E. Lebensohn.

Berliner, M. L. **Cornea and sclera.** A.M.A. Arch. Ophth. **45**:196-223, Feb., 1951.

In this annual review of the current literature on the cornea and sclera, the anatomy and embryology, physiology, pharmacology, experimental pathology, corneal and scleral disease and their treatment are discussed and new developments in keratoplasty are described.

John C. Long.

Ching, Renald. **Aureomycin in the treatment of trachoma.** A.M.A. Arch. Ophth. **45**:657-665, June, 1951.

Data on a series of 44 selected trachoma patients hospitalized in Hong Kong for aureomycin treatment are tabulated to show the effect of the antibiotic. Aureomycin had a marked beneficial effect in all the cases in which the drug was employed. The combined local and systemic administration appeared to give a higher percentage of good results and more rapid improvement. The severer the inflammatory condition of the eye, the more dramatic was the result. Ambulatory patients with little inflammation showed no improvement and no regression of the manifestations of trachoma. The author believes that aureomycin has no effect on trachoma itself but is a valuable drug in that it promptly eliminates the secondary organisms that cause much of the destruction. John C. Long.

Ciotola, G. **The alleged effect of urea in treating herpetic keratitis.** Boll. d'ocul. **30**:417-423, July, 1951.

Glycerine-preserved herpes virus was inoculated into the corneas of seven rabbits. After 24 hours a 25-percent solution

was instilled into the distended conjunctival sac and kept there for 5 to 10 minutes. Treatment was repeated on alternate days. The results are reported in tables which show the intensity of corneal infiltration, conjunctival discharge and congestion of the iris. Two animals were given subconjunctival injections of the same solution daily and both the instillations and injections were well tolerated, although large defects in the corneal epithelium remained 24 to 48 hours after the instillations. Four of the animals died of encephalitis 8 to 10 days after the inoculation. Three animals were not treated at all. Treatment with urea did not influence the course of the corneal disease in the experimental animals and no beneficial results were obtained in four patients who had superficial herpetic keratitis. K. W. Ascher.

Cogan, D. G. **Recurrent bilateral scleritis of many years' duration with unusual corneal infiltration (fat?).** A.M.A. Arch. Ophth. **46**:341-342, Sept., 1951.

This case is of interest because the condition has persisted for 18 years and is accompanied with unusual corneal opacities. It has also provided an unusual opportunity to try a variety of therapeutic procedures none of which were beneficial. It appears to be clinically the same entity as that described by Uhthoff.

R. W. Danielson.

Contardo, Rene. **Trachoma in Chile.** Rev. intern. du trachome **28**:348-352, 1951.

Contardo enlarges on a report given to the Pan-American Congress in 1945. Only 2,732 cases of trachoma have been noted among the five million inhabitants of Chile. The peak of 0.58 percent is reached in the southern area.

James E. Lebensohn.

Ellman, P., Weber, F. P., and Goodier, T. E. W. **Contribution to the pathology of Sjögren's disease.** Quart. J. Med. **20**:33-42, Jan., 1951.

Sjögren's disease consists of a chronic inflammatory atrophy involving the salivary, lacrimal, mucosal and sweat glands. The condition gives rise to obstruction of the ducts and secondary inflammation. The glands are replaced by more or less dense, poorly-defined aggregates of small lymphocytes, the blood vessel walls are thickened with hyaline connective tissue and the ducts are blocked. Even the glands of the Moll are atrophied and enveloped by lymphocytes. A case of the disease with postmortem, especially histological examination, is described. (7 photomicrographs) Orwyn H. Ellis.

Farnarier, G., Guillot, P., and Bona, J. **Evolution of corneal grafts in trachomatous eyes.** Rev. intern. du trachome **28**: 303-308, 1951.

In five cases of corneal grafts, performed in old cases of cicatricial trachoma, the keratoplasties were lamellar in four, and total in one. All the grafts were well tolerated. The final results showed that in lamellar keratoplasty some secondary vascularization slips under the graft, but in total keratoplasty vascularization stops at the limbus. Total keratoplasty is therefore preferable in these cases. James E. Lebensohn.

Gibson, J. B. Gilchrist. **Recurrent pterygium.** M. J. Australia **11**:664-669, Nov. 17, 1951.

In 240 patients with pterygium, there was recurrence in 20 percent and revascularization of the corneal scar in 30 percent. Microscopic examination of the heads of the pterygia revealed no histologic changes to indicate a tendency toward recurrence. Recurrences are less frequent in older persons than in the young. Vascularity is associated with a high incidence of recurrence. X-ray treatments were given to 18 patients and in no case

was there revascularization as long as five months after irradiation. The technique for protecting the cornea with a lead contact lens is described in detail and the dosage is given. The author believes that this method is preferable to repeated transplantations of the pterygium. (2 tables, 13 figures) H. C. Weinberg.

Larmande, A., and Toulant, M. **Lesions of the smooth levator muscle of Müller in trachomatous ptosis.** Rev. intern. du trachome **28**:299-302, 1951.

The authors showed that the smooth levator muscle of Müller plays an important role in the development of trachomatous ptosis and demonstrated an interstitial myositis with sclerosis within this muscle. James E. Lebensohn.

Lowe, Ronald F. **Louse-bite conjunctivitis.** M. J. Australia **2**:295-296, Sept. 1, 1951.

A unilateral allergic conjunctivitis followed the bites of Pediculus humanus along the left upper lid edge. Nits were present on the lashes of only one eyelid. The incubation period for nits varies according to the temperature but is about one week. The larva feeds on the host's blood as soon as it emerges. The bite sets up itching and the appearance of an urticarial weal, spreads from the lid margins and produces allergic conjunctivitis.

"Lorexane" head lotion contains 0.2 percent gamma isomer of benzene hexachloride (BHC), which is a powerful insecticide stated to be 20 times as potent as DDT. The head lotion is applied directly to the affected hair and skin and the area is left unwashed for 7 to 10 days. Any larvae which may subsequently develop from the nits are then destroyed. One painting of the lotion effected a rapid cure in the present case.

Theodore M. Shapira.

Mitsui, Y., Tanaka, C., Toya, H., Iwashige, Y., and Yamashita, K. **Terramycin in the treatment of trachoma.** A.M.A. Arch. Ophth. **46**:235-244, Sept., 1951.

The authors reviewed the results of treatment with terramycin in about 700 cases of trachoma. Early trachoma, of less than two-months' duration, always responded promptly and well. A 0.1-percent terramycin hydrochloride ointment, or a 0.5-percent solution applied more than four times a day produced a clinical cure in a few weeks. Chronic trachoma of several years' duration responded fairly well. A 0.5-percent ointment applied three times a day for four weeks was followed by cure in about 80 percent of cases and a combination of surgical and terramycin therapy gave far better results. Acute pannus and ulceration of the cornea responded promptly to this treatment. In pannus crassus, however, two weeks' treatment was required before healing was complete, even with a larger dose. In all these conditions, systemic administration alone seemed to have little advantage over topical application, and ointment was slightly more effective than a solution.

R. W. Danielson.

Nosik, W. A., and Johnson, L. V. **The treatment of bullous keratitis by greater superficial petrosal neurectomy.** J. Neurosurg. **8**:498-503, Sept., 1951.

Greater superficial petrosal neurectomy has been effective in relieving the symptoms and signs of severe chronic bullous keratitis by the restoration of a more normal balance of osmotic tension of the precorneal film and the corneal stroma. After operation the patients usually are ambulant on the first or second day and are ready to leave the hospital on the fourth or fifth day. There is an immediate decrease in the ocular pain and in lacrimation as evidenced by the Schirmer test.

The corneal bleb formations, bullae and edema, and the angry redness, which was a prominent feature pre-operatively, subside within a few days. As the healing of the residual corneal abrasions proceeds, vision begins to improve. In two patients the visual acuity in the affected eye was 20/300 before operation and 20/30 four weeks later, with only a mild degree of conjunctival injection. Where corneal opacity remains because of necrotic epithelium, secondary corneal stripping may be necessary to gain maximal visual acuity even after favorable osmotic tension has been established.

Theodore M. Shapira.

O'Day, Kevin. **Bengal rose as an aid in the diagnosis of "kerato-conjunctivitis sicca" (Sjögren's syndrome).** M. J. Australia **2**:708-709, Nov. 24, 1951.

Bengal rose is a water-soluble eosin dye and is used in the eye in a solution of one-percent chloretone water. One drop, washed out after 30 seconds with normal saline, will show small red dots on the conjunctiva or cornea wherever epithelium is desquamating. When clusters of staining points are seen on the conjunctiva and cornea, the diagnosis of keratoconjunctivitis sicca is probable. The author has had excellent results over a period of 10 years with this test and recommends it especially in the diagnosis of chronic conjunctivitis.

H. C. Weinberg.

Pagliarini, N. **Clinical contribution to tuberculosis of the conjunctiva.** Boll. d'ocul. **30**:404-416, July, 1951.

Three cases of tuberculosis of the conjunctiva, one of them a primary infection, are reported. There are three photographs and a discussion of the differential diagnosis and of modern therapeutic achievements. In all three patients, girls of 12 and 14 years and a 27-year-old man, recovery was complete. (References)

K. W. Ascher.

Poleff, L., and Viennot-Bourgin, M. **Viroscopic detection of trachoma carriers.** Rev. intern. du trachome **28**:338-343, 1951.

Inclusion bodies can be found in all stages of trachoma. The microscopic confirmation of the diagnosis is facilitated by the citrated methylene blue stain of Poleff, the technique of which is extremely simple. After fixing the conjunctival scraping by flaming, the dye is applied for three minutes and then washed off in running water. The cells with the inclusion bodies stain reddish-violet and show clearly against the light blue background. In a study of 500 Moroccan school-children, the Poleff stain revealed inclusion bodies in 94.5 percent of eyes clinically diagnosed as trachoma, and in 42.3 percent of those considered dubious or unaffected. James E. Lebensohn.

Sakon, H., Kohn, M., and Raphael, E. R. **The treatment of trachoma by aureomycin and chloromycetin.** Rev. intern. du trachome **28**:309-324, 1951.

In Morocco, over half of all ocular ailments are due to trachoma. These workers for the Oeuvre de Secours aux Enfants (OSE), a French-Jewish agency now subsidized by Americans, present a detailed report on 90 cases in children and adults in which the results of antibiotic therapy are carefully evaluated. The systemic use of aureomycin and chloromycetin was without benefit. When ointments of penicillin (5,000 U. per gram), instilled every two hours day and night, aureomycin (2½ percent) and chloromycetin (5 percent) were used, the inflammatory signs progressively subsided and cicatrization was accelerated. In initial trachoma the follicles disappeared more or less com-

pletely but in florid trachoma (stage II) a papillary infiltration persisted. Pannus was not affected. All the patients were observed for two months after cessation of treatment, and remissions were noted in only two cases. Epithelial inclusion bodies cannot be detected after 5 to 15 days, depending on the concentration of the medication used. James E. Lebensohn.

Siltzbach, L. E., Posner, A., and Medine, M. M. **Cortisone therapy in sarcoidosis; effect in a case with virtual blindness.** J.A.M.A. **147**:927-939, Nov. 3, 1951.

A 30-year-old Negro woman had generalized sarcoidosis with extensive and severe bilateral ocular lesions of a month's duration. The vision had deteriorated so much that she had to be led about. Visual improvement began from the first day of cortisone therapy, which was given for 15 weeks. At the time of discharge she had 76 percent normal binocular vision. She was given 150 mg. daily for the first 3 weeks, then 100 mg. for the 4th and 5th weeks, 75 mg. for the 6th and 7th weeks (there was a shortage of the drug), and from the 8th to 15th weeks 150 mg. In the final week the dosage was tapered off. The original lesions in the eyes consisted of ciliary injection, corneal opacities, cloudy vitreous, and unpigmented keratic precipitates. (4 figures, reference)

Bennett W. Muir.

Swan, K. C. **Some contemporary concepts of scleral disease.** A.M.A. Arch. Ophth. **45**:630-644, June, 1951.

The sclera should be considered an intercellular collagenous tissue which may be, and often is, affected by many of the local and systemic disease processes that affect such tissues. Classification of scleral inflammation on the basis of tissue response may include proliferative and exudative scleritis, scleritis associated with fibrinous degeneration, and physical or chemical changes resulting from injury and scleropathies. Examples of various types of scleral disease are reported. (9 figures) John C. Long.

Weinstein, P., and Forgács, J. **Conjunctival angioscopy.** Brit. J. Ophth. **35**:479-483, Aug., 1951.

With high magnification photography, three forms of aneurysms could be distinguished: a saccular type occurring in arteriosclerosis and usually situated at the bifurcation of the vessels, a fusiform type seen in hypertension, and a berry-shaped type occurring mainly in diabetes. Over short periods these aneurysms were seen to change shape and the authors concluded that aneurysmal dilatation is an expression of functional vasomotion, and may serve to secure an even blood supply within the capillaries. (9 figures)

Orwyn H. Ellis.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Bárány, Ernst. **Rate of flow of aqueous humor in normal and scorbutic guinea pigs.** A.M.A. Arch. Ophth. **46**:326-336, Sept., 1951.

The rate of flow of aqueous humor was determined in unanesthetized guinea pigs which had been given widely different amounts of ascorbic acid. There was no difference in rate of flow despite large differences in aqueous ascorbic acid unless the animals had severe scurvy. Rate of flow was about 1.7 percent of the volume of the anterior chamber per minute in normal guinea pigs and about 1.4 percent per minute in animals with marked scurvy. (9 tables)

R. W. Danielson.

Becker, B., Linner, E., and Bárány, E. **Rate of turnover of ascorbic acid in aque-**

ous humor in rabbits. A.M.A. Arch. Ophth. **45**:653-656, June, 1951.

The rate of turnover of ascorbic acid in the aqueous of rabbits under urethan anesthesia was determined by a method which utilized the fall and rise in ascorbic acid following alternate occlusion of the carotid arteries. The values obtained were 1.3 to 1.5 percent per minute. (2 charts)

John C. Long.

Grant, W. M. **Clinical measurements of aqueous outflow.** A.M.A. Arch. Ophth. **46**: 113-131, Aug., 1951.

Measurements were made by a tonographic method with an electric tonometer and recording galvanometer, to test the facility with which the aqueous can be expressed from the eye, and the rate of formation of aqueous in eyes under steady-state conditions was calculated. Morton believes that the increase in intraocular pressure in glaucoma is practically always, possibly exclusively, caused by increased resistance to outflow of aqueous from the eye, and not by hyperformation of the aqueous. The beneficial effect of surgical and medical treatment in glaucoma is achieved principally through improving the facility of aqueous outflow. In the discussion, Dr. Jonas S. Friedenwald develops the mathematical formulae by which the tonometric data may be converted.

John C. Long.

Jancke, G. **Sympathetic chorioretinitis as a neurogenic disease.** Klin. Monatsbl. f. Augenh. **119**:370-378, 1951.

Four cases of disseminate chorioretinitis in one eye developed many years after the other eye had been injured. Although a neurogenic pathogenesis may be considered, it remains undecided whether or not this condition is identical with typical sympathetic ophthalmia.

Ernst Schmerl.

Joy, H. H. **Sympathetic ophthalmia, its pathogenesis and prophylaxis.** New York State J. Med. **51**:2613-2616, Nov. 15, 1951.

Prevention is of paramount importance and the prompt removal of hopelessly injured eyes is strongly advised. Where an injured eye is retained, with the hope of restoring sight, any uveal prolapse should be promptly and completely removed. Cautery is to be avoided. The decision for late enucleation depends on the presence of long standing low-grade uveitis with exacerbations, particularly if phthisis seems inevitable. The incubation period of the disease is limitless and prophylactic enucleation should not be delayed too long when an eye is blind. An eye with only light perception should not be removed if the vision in the fellow eye is seriously impaired by inflammation without a careful study of the type of injury and type of uveitis in the second eye. Atropine and systemic care are important but ACTH is too new to be relied upon.

F. M. Crage.

Korff, Jürgen. **Difficulties in the differential diagnosis between inflammation and tumor.** Klin. Monatsbl. f. Augenh. **119**:378-388, 1951.

Three cases of iridocyclitis which had been considered tuberculous are discussed to show the difficulties in making a differential diagnosis. When the clinical course of a supposedly granulomatous iridocyclitis is atypical it may be a malignant tumor and biopsy may be necessary to establish a diagnosis. (10 figures)

Ernst Schmerl.

Linhart, W. O. **Induced ocular tuberculosis.** A.M.A. Arch. Ophth. **46**:271-276, Sept., 1951.

A student nurse had been given BCG vaccine and an injection of OT which was followed several weeks later by acute iritis and uveitis. Vision in the right eye was

6/200 and in the left reduced to light perception. In the two years during which the patient has been observed she has had recurrent attacks of ulcerative colitis, probably tuberculous, and an interstitial keratitis which healed but left a corneal scar. Final vision in the right eye was 20/50, in the left, light perception.

R. W. Danielson.

Rohrschneider, Wilhelm. **Spontaneous serous detachment of the anterior choroid.** Klin. Monatsbl. f. Augenh. **119**:337-350, 1951.

The patient's right eye had been removed after a diagnosis of an intraocular tumor, which was not confirmed histologically. Two years later, myopia developed in the remaining eye, with narrowing of the visual field, especially from the sides. The aqueous became opaque, the iris hyperemic and the fundus indistinct, but the papilla seemed normal. Vision, which had been normal, was slightly less than 20/40 with a correction. The preliminary diagnosis was iritis and retinal detachment. After a few days the iritis improved and the fundus became visible. There was vertical bulging into the vitreous to both sides of the papilla and a pattern of streaks on diascleral transillumination. A bright luminescent circle surrounded the tip of the transilluminator where it touched the sclera. The diagnosis of choroidal detachment was made. Conservative treatment and dehydration caused only temporary improvement; repeated scleral punctures, electrodiathermy and withdrawal of the subchoroidal fluid seemed to be of benefit. However, four months after the last operation, vitreous opacities increased and interfered with the patient's vision. The ocular tension varied between 15 and 20 mm. Hg Schiøtz. The pathogenesis of the spontaneous detachment of the choroid is not known but shrinkage of the vitreous might be a factor. Ernst Schmerl.

9

GLAUCOMA AND OCULAR TENSION

Langley, D., and Swanljung, H. **Ocular tension in glaucoma simplex.** Brit. J. Ophth. **35**:445-458, Aug., 1951.

Thirty-six cases of chronic simple glaucoma are analyzed and the twenty-four hour tension curves, field changes, blood pressure, provocation tests and other relevant factors are discussed. The double variation curve was found more frequently than all other types. Most of the patients had similar curves when retested some months later. In many cases of glaucoma simplex the tension was less than 30 mm. Hg (Schiøtz). Eyes with greater maximum tension usually had greater field defects. In general, the higher the ocular tension, the greater the variations. The variations of tension in the two eyes of an individual were remarkably parallel although differing in degree. A correlation between blood pressure and ocular tension was found in only one case. The authors believe that ocular movements are responsible for changes in tension, but no relationship could be shown to body posture or meals. The tension curve gives more information than provocation tests and provides a useful manner of deciding upon the best time for treatment in cases of diurnal variations. It is also a reliable method of assessing the results of operation. Tensions taken from 5 a.m. to 7 p.m. are usually sufficient to record the maximum tension. (12 figures)

Orwyn H. Ellis.

Muldoon, W. E., Ripple, P. H., and Wilder, H. C. **Platinum implant in glaucoma surgery.** A.M.A. Arch. Ophth. **45**: 666-672, June, 1951.

Platinum wire was implanted into several locations of the rabbit eye. The metal was well tolerated except when in contact with the ciliary body. The rather severe pathological changes noted when the im-

plant was placed in contact with the ciliary body seem to indicate that this region is an unfavorable site for an implant. In two patients with glaucoma a platinum wire implant was used as a seton. In both there has been satisfactory control of the glaucoma and no inflammation for over two years. This procedure is not recommended to supplant other operations for glaucoma, but the feasibility is demonstrated. John C. Long.

Pereira, R. F. **Diathermy in the surgical treatment of glaucoma.** Semana méd. **99**: 536-539, Sept. 20, 1951.

In nine cyclodiathermy operations performed on seven patients, the eye was anesthetized with a retrobulbar injection of 1 cc. of novocaine. The punctures were made with a López Lacarrère electrode. The wire penetrated about 1 mm. at 8 to 9 millimeters from the limbus and the intensity was about 30 to 35 milliamperes. About 20 punctures were made and the electrode was pressed through the conjunctiva and sclera for 10 seconds for each puncture. At the end of the operation, the author advises either two penetrating punctures or a paracentesis of the anterior chamber.

In six of the cases the tension has been normal since operation, with pilocarpine instillations in five and without medication in one. Two eyes had some irritation of the iris, in one of them a higher intensity (50 ma.) had been used and in the other the punctures were made 6 mm. from the limbus. The operation is recommended because of its simplicity and its safety. (1 figure, 5 references)

A. Arruga.

Wilson, E., and Swift, S. H. **Cortisone in the treatment of secondary glaucoma.** M. J. Australia **2**:598-599, Nov. 3, 1951.

A man, 37 year old, was treated for a low-grade, intractable rheumatic fever associated with anemia, carditis and polyarthritis. There was also glaucoma, secondary to an acute iritis. The inflammation and high tension in the eye did not respond to the ordinary treatment for iritis but after 24 hours of cortisone the cornea cleared, adhesions broke and the tension returned to normal. The glaucoma and iritis remained cured even after cortisone was discontinued after four days. A temporary remission of the rheumatism had occurred, and the vision returned to normal. F. M. Crage.

10

CRYSTALLINE LENS

Cordes, F. C. **Evaluation of the surgery of congenital cataracts.** A.M.A. Arch. Ophth. **46**:132-144, Aug., 1951.

The surgical prognosis in congenital cataract is not as good as it is in senile cataract, as other congenital anomalies may complicate the surgery. In only 50 percent is postoperative vision of 20/200 or better achieved, so that if a child has vision of 20/50 the cataract should probably be left. The age, indications, technique and complications of congenital cataract surgery are discussed. The author prefers linear extraction with the injection of air into the anterior chamber and this method is given in detail, with suggestions for modification to meet special requirements. John C. Long.

Montresor, Dante. **Surgical treatment of luxations of the lens.** Rassegna ital. d'ottal. **20**:139-162, May-June, 1951.

The numerous theories which attempt to explain the causes of subluxation and luxation of the lens and the signs and symptoms resulting from these defects are reviewed. The various surgical measures which have been and still are recommended by the many writers on the subject are presented and criticized, mostly unfavorably. The method of Franceschetti of discission of ectopic and dislocated

lenses is praised, and the results obtained in seven cases are presented.

Eugene M. Blake.

11

RETINA AND VITREOUS

Cartasegna, Federico. **The treatment of retinal venous thrombosis with dicumarol.** Rassegna ital. d'ottal. **20**:163-171, May-June, 1951.

The author concludes that the employment of dicumarol is effective in recent thrombosis especially in comparatively young individuals. In longer standing thromboses, where there is considerable sclerosis of vessels, it is less favorable. The improvement consists principally in a more rapid absorption of retinal bleeding and in the restoration of better circulation with consequent improvement in visual acuity. Eugene M. Blake.

Eggers, Harry. **Lipotropic substances for the absorption of vitreous opacities.** New York St. M. J. **51**:2255-2256, Oct. 1, 1951.

Patients apparently in good health often show noninjected eyes in which vitreous floaters have appeared rather suddenly. In most instances no spot of choroidal or retinal inflammation can be seen with the ophthalmoscope. These opacities, when not associated with constitutional diseases, are the result of recent or present, low-grade, often intermittently active, focal infection. Any focus of infection should be eliminated and the ophthalmologist should attempt to influence the absorption or regression of these vitreous infiltrates. In a number of cases of vitreous clouding or opacities, the ingestion of lipotropic substances definitely promotes the disappearance of the clouding and the absorption of the smaller opacities. Although large strands and fibrillae usually do not disappear, they may shrink. On rare occasions the large floaters disappear. Not all patients respond to lipotropic substances, especially not those with active focal or constitutional infection. The mode of action of these substances is not known, but Eggers believes that the vitreous clears more completely and faster than without their use.

Theodore M. Shapira.

Feigenbaum, Aryeh. **Familial detachment of the retina and the question of interruption of pregnancy because of juvenile idiopathic detachment.** Boll. d'ocul. **30**:195-199, Aug.-Sept., 1951.

Familial juvenile idiopathic retinal detachment occurred in three generations of a family. A woman of the second generation, 32 years old, blind in one eye and with a reattachment in the other went through pregnancy and labor without further harm to her better eye. Her child developed retinal detachment in one eye when 13 years old and in the other when 15, and both eyes were successfully healed by surgical operation. Nine other young women with past or present detachment went through 17 pregnancies without harmful effects on the eyes. The author believes that pregnancy is not contraindicated because no direct trauma results from labor. Eugenic considerations alone should be of importance in advising against childbearing. F. M. Crage.

François, Jules. **The retinal circulation in congenital cardiopathology.** Rassegna ital. d'ottal. **20**:121-127, May-June, 1951.

The writer examined three cases of the tetralogia of Fallot, two of Eisenmanger disease (high interventricular communication), and three of stenosis of the tricuspid. All had had catheterization of the heart and all had cyanosis. Three noncyanotic patients with uncomplicated interventricular communication (Roger's disease) were studied. The following observations were made: patients with

cyanosis showed dilatation and tortuosity of the retinal veins as the first and most important sign. In pure pulmonary stenosis, a lesser venous dilatation was observed. These anomalies co-existed with cyanosis of the skin and mucous membranes. The number of red cells may be greatly increased and the hemoglobin may be as high as 110 percent. In Vaquez disease, the venous dilatation resulted from anoxia. In six cases observed, dynometric compression of the globe produced no collapse of the veins but did produce a prolonged venous pulse. (19 figures)

Eugene M. Blake.

Friedman, M. W. **Occlusion of central retinal vein in migraine.** A.M.A. Arch. Ophth. **45**:678-682, June, 1951.

The reported cases of permanent vascular damage to the eye as a complication of migraine are listed, and the case of occlusion of the central retinal vein associated with migraine seen by the author is described. The symptoms of migraine probably result from the alteration of the caliber of the blood vessels in the head and both intracranial and extracranial vessels take part in this process. Possibly the repeated vascular explosions attending migraine may give rise to a rather localized atherosclerosis. John C. Long.

Gomes daSilva, Avelino. **Angioid streaks.** Arq. brasil. de oftal. **14**:70-82, 1951.

The author comprehensively reviews the history of this unusual condition from 1889, when Doyne described the ophthalmoscopic findings for the first time. Subsequent investigators demonstrated the association with macular degeneration and pseudoxanthoma elasticum.

A brownish halo surrounding the disc is believed to be pathognomonic of the syndrome, and may be present for some time before its true identity is revealed by the development of streaks which radiate from it and characterize the disease. The streaks may be narrow or broad, very irregular and dark, light, or reddish in color. The macular region, when affected, undergoes pigmentary degeneration resembling that seen in senility or in some cases of myopia. The pigmentation progresses until it assumes a mosaic aspect. Retinal hemorrhages or exudation may eventually occur. The latter changes produce metamorphopsia, central scotoma, or central blindness. The degenerative phenomena support the belief that the disease may be considered a retinal abiotrophy. Pigment deposits in the equatorial and peripheral zones of the retina constitute the third area of involvement. A large circle of pigment is formed, the external border of which marks the limit of the radiating streaks. Visual symptoms apparently are not produced by the equatorial changes, and the retina beyond this zone is considered to be normal. Angioid streaks are always bilateral and are a symptom of a general disease, although the eye findings may be in a more advanced stage of evolution. The streaks are not in the retina (the retinal vessels pass over them), but in the choroid.

The syndrome affects both sexes, is found most frequently between the ages of 30 and 50 years and appears to be hereditary and recessive. Trauma, syphilis, tuberculosis, and alcoholism have been considered as possible causes.

Several theories have been offered to account for the formation of the streaks. Tears in Bruch's membrane are the most widely accepted substratum and this explains the association of the eye lesion with pseudoxanthoma elasticum, or the Grönblad-Strandberg syndrome, a systemic affection of elastic tissue. The streaks are also found in conjunction with senile elastosis, Paget's disease of the

bone, syphilis, trauma, diabetes, and tuberculosis. Unfortunately, few specimens have been examined histologically. Therapy is ineffective. (3 figures, one in color) James W. Brennan.

Krümmel, H. **The localization of retinal tears in idiopathic retinal detachment.** Klin. Monatsbl. f. Augenh. **119**:388-400, 1951.

In 523 idiopathic retinal detachments the right eye was affected in 60 percent, the left eye in 40 percent; 66 percent of the retinal tears in the right eye and 57 percent in the left were found in the upper temporal quadrant. Presumably because of the stresses produced by the attachment of the superior oblique muscle to the eyeball, this is the area primarily involved. (10 figures, references)

Ernst Schmerl.

Magni, S. **Patherogometry in retinal detachment.** Boll. d'ocul. **30**:457-476, Aug., 1951.

In 54 patients with detachments of different types, the allergy against tubercule bacilli was determined by Gröer's quantitative method. More than one-fourth of all patients showed no sensitiveness to tuberculin; less than half of them are listed as pleoergically heterodynamic; less than one-fourth as pleoaesthesically heterodynamic, and about 1/20 homodynamic. While the results did not reveal any relation between pathergy and type of retinal detachment, the author suggests that in these patients general treatment should aim at improvement of humoral and tissue defence. (References)

K. W. Ascher.

McDonald, P. R. **Cause of failure in retinal detachment surgery.** A.M.A. Arch. Ophth. **45**:645-652, June, 1951.

Of 88 cases in which operation was performed for detachment of the retina, the results in 24 were listed as failures. Prognosis was influenced by the size of the tear, the duration of the detachment, the condition of the retina and vitreous, the presence of high myopia and aphakia and the presence of uveitis. Retinal tears were found in 86 percent of the successful cases and in only 33 percent of the unsuccessful. The two most important factors contributing to failure were inability to locate the tear in the retina and disorganization of the retina and vitreous. Many valuable points in treatment are mentioned.

John C. Long.

Schupfer, F. **Retinosis pigmentosa following an acute infectious disease.** Boll. d'ocul. **30**:424-432, July, 1951.

A 43-year-old man had had typhoid fever 33 years previously during two months of which bilateral amaurosis was present. He slowly recovered his vision and was able to continue with his school work. Fifteen years later, the diagnosis of retinosis pigmentosa was made and confirmed by various eye specialists. Recent findings in the lens and fundus of both eyes were characteristic of this disease except for extremely dense pigmentation in the periphery. Corrected vision was 5/15 in the right and 5/7.5 in the left eye; typical ring scotomas were present. Toxic action of the microorganisms or an allergy might be considered, as the inciting factor. (References) K. W. Ascher.

Tansley, Katharine. **Hereditary degeneration of the mouse retina.** Brit. J. Ophth. **35**:573-582, Oct., 1951.

In an albino stock of mice with a retinal degenerative lesion as a recessive Mendelian character, no other abnormalities, not even cataract, were observed. The eyes were examined microscopically from birth to 15 months of age. The retina appeared to develop normally until the animals were 14 days old although

differentiation of the inner nuclear layer was slightly delayed. The lesions were always bilateral and progressed at about the same rate in the two eyes and in different animals. The first sign of abnormality was the appearance of pyknotic cells in the outer nuclear layer of the central retina. These degenerations spread to the periphery, and the outer nuclear layer was thinned in the center. After the 16th day the rods gradually lost their characteristic structure. By the 21st day nothing but debris could be seen between the external limiting membrane and the pigment epithelium. At four weeks there was no sign of the rods, except an occasional nucleus, the external limiting membrane could be seen only in places, and part of the pigment epithelium was swollen and abnormal. After the 4th week some retinas progressed quickly and others slowly to serious disorganization. At nine weeks the choroid varied in appearance between a sclerosed thickening and disappearance, yet there were areas where the pigment epithelium and choroid appeared fairly normal. In the late stages gliosis was marked. The lesion is compared to retinal degenerations as described in man and other animals and resembles pseudoretinitis pigmentosa. It might be considered as an abiotrophy. (11 photomicrographs)

Orwyn H. Ellis.

12

OPTIC NERVE AND CHIASM

Montanelli, Mario. **Bilateral calcification of internal carotid artery.** Riv. oto-neuro-oftal. **26**:119-127, March-April, 1951.

A woman, 69 years old, had marked diminution of vision and sclerosis of the retinal blood vessels in both eyes. Later both discs were white, not excavated, with net margins, and all branches of the central artery became filiform, contained no blood, and appeared like white cords. Signs of general arteriosclerosis were present and X-ray films showed a rosary-like calcification of the internal carotid arteries. The condition was apparently due to sclerosis of the retinal blood vessels and not to pressure on the central artery of the optic nerve. Treatment with iodine had caused a temporary improvement of symptoms; this improvement could not have occurred had the symptoms been ascribable to pressure only. The retina had been totally deprived of circulating blood, brought about not by compression of the central artery but through lack of a proper supply of blood for the nutrition of the optic nerve and retinal elements. (4 figures, 24 references)

Melchior Lombardo.

13

NEURO-OPHTHALMOLOGY

Adler, F. H. **Optic atrophy, uveitis and intracranial disease.** A.M.A. Arch. Ophth. **45**:683, June, 1951.

The patient, a 21-year-old man, had the unusual combination of optic atrophy in one eye, uveitis with cecocentral scotoma in the other eye, lymphocytosis in the spinal fluid and neurologic evidence of an intracranial lesion. Basal arachnoiditis seemed to be the most probable diagnosis.

John C. Long.

Borges Dias, A. **Herpes zoster ophthalmicus.** Arq. brasil de oftal. **14**:67-69, 1951.

A brief review of this serious disease is presented with a case history, unusual by virtue of the patient's age, 13 years. Previous authors indicate that adults of middle age are most often affected. There are erythema and edema of the facial region supplied by the ophthalmic division of the fifth cranial nerve, neuralgic pain, vesicles and crusting of the vesicles as well as fever, chills, nausea, vomiting and anorexia. The limitation of the eruption by the midline of the face is of diagnostic importance. The eye itself is affected in a

high percentage of patients who complain of photophobia, lacrimation, pain, and blepharospasm and impaired vision. Vesicles are rarely seen on the eye itself.

The 13-year-old child, in whom effection of the eye was minimal was treated with aureomycin and sulfadiazine, and made a rapid and uneventful recovery.

James W. Brennan.

Chamlin, M., and Davidoff, L. M. **Divergence paralysis with increased intracranial pressure.** A.M.A. Arch. Ophth. **46**: 145-147, Aug., 1951.

The authors report a total of 15 cases from their observation or from the literature in which increased intracranial pressure was associated with a divergence paralysis. The only common factor was the increased intracranial pressure and the paralysis. In 10 of the cases there was definite improvement in the paralysis following relief of the increased intracranial pressure. While the presence or absence of a true divergence center is unanswered, the present observation would argue against, rather than for, the existence of such a center. If divergence paralysis is encountered, increased intracranial pressure should be suspected and sought, even in the absence of papilledema.

John C. Long.

Oppenheimer, H., and Weissman, M. **On anosognosia: report of a case of anosognosia for blindness.** Am. J. Psychiat. **108**:337-342, Nov., 1951.

The case discussed had a Korsakow type of psychosis and a persistent anosognosia for his blindness. The blindness was thought to be of central origin and the anosognosia the result of diffuse cortical disease; a "functional" cortical localization was considered more appropriate than a "topographic" one. Orwyn H. Ellis.

Teuber, H.-L., Battersby, W. S., and Bender, M. B. **Performance of complex visual tasks after cerebral lesions.** J. Nerv. and Ment. Dis. **114**:413-429, Nov., 1951.

A study of specific intellectual deficits after lesions in the frontal lobes four to seven years after injury is based on 131 World War II veterans all of whom had had loss of cerebral substance from penetrating missiles. The testing was done by means of a complex system of "hidden figures", "sorting tests" and similar methods. These highly specialized tests which involve complex visual discriminations showed characteristic deficits but the deficits found were equally pronounced after penetrations of frontal and of posterior lobe substance. From these studies it would seem that complex visual discriminations are not entirely dependent upon the integrity of the frontal lobes but depend to an even greater extent on the integrity of the posterior (parieto-temporo-occipital) regions. The older concept has been that loss of frontal tissue produces unique intellectual changes. It has been assumed that the prefrontal areas represent the specifically human part of the primate brain. Intellectual functions of brain tissue cannot be determined by comparative anatomy nor by histologic study but only by systematic behavioral studies. (64 references) Claude L. LaRue.

14

EYEBALL, ORBIT, SINUSES

Field, H. B. **Foreign body (curtain rod) penetrating orbit, pharynx, and neck, with complete recovery.** A.M.A. Arch. Ophth. **46**:157-158, Aug., 1951.

A curtain rod, ¼ in. in diameter and 20 in. in length, was forced into the left orbit by a fall. The rod penetrated to a depth of 15.5 cm., and was visible under the skin of the neck at the left side of the atlas. Its surgical removal was followed by complete recovery. John C. Long.

Fralick, F. B. **The orbit.** A.M.A. Arch. Ophth. **46**:343-359, Sept., 1951.

This is an excellent review of the literature of the orbit for the past year

R. W. Danielson.

15

EYELIDS, LACRIMAL APPARATUS

Ainslie, D. **The treatment of blepharitis.** Brit. M. J. **2**:582-584, Sept. 8, 1951.

The results of treatment with aureomycin of 30 cases of long-standing blepharitis and the initial results in two cases treated with terramycin are discussed. Because of the danger of allergic responses antibiotics should be reserved for cases which have failed to respond to the older methods of treatment. Empirical remedies, such as mercurial ointments, are often effective, but when there is little or no improvement, a culture and a sensitivity test should be made and the most appropriate antibiotic chosen. In this way, prolonged ineffective treatment will be avoided and the danger of allergic responses minimized. Once treatment with an antibiotic is decided upon, it must be conducted with the utmost vigor so that the danger of producing insensitive strains of the organism will be reduced to a minimum.

Theodore M. Shapira.

Gibson, J. B. Gilchrist. **Congenital obstruction of the nasolachrymal duct: a review of 130 cases.** M. J. Australia **11**:764-766, Dec. 8, 1951.

Congenital epiphora was bilateral in 12 percent of 130 cases. Conservative treatment should be tried for a few weeks in the majority of cases. If probing is necessary, a narrow straight probe with a blunt acorn end is best. The lower punctum is most often used and no false passage was obtained in any case. Repeated probings which were necessary in 6 percent of the cases should not be done until at least four weeks have intervened. The hollow probe technique, where a horse-hair suture or a length of silkworm gut is passed through the probe has been found most satisfactory. The suture is passed through into the pharynx because the angle of the naso-lachrymal duct tilts backwards at an angle of 20 degrees. (2 figures)

H. C. Weinberg.

17

INJURIES

Jones, A. C. **Emergency surgery and emergency treatment of eye burns.** Northwest Med. **50**:769-770, Oct., 1951.

A general outline for care of injuries, lacerations and fractures of the face is given. Careful approximation of all wounds, early reduction of fractures and care of eye burns is discussed and the use of hydrosulphosol is emphasized as the treatment of choice in all burns.

Orwyn H. Ellis.

18

SYSTEMIC DISEASE AND PARASITES

D'Ermo, F. **Ocular changes in Paget's disease.** Boll. d'ocul. **30**:477-488, Aug., 1951.

To the known cases of eye conditions connected with osteitis deformans, two more are added. They were observed in the Rome University Eye Clinic, in women aged 67 and 64 years. Both patients were admitted for visual disturbance, attributable in one case to mature cataract and bilateral arteriosclerotic macular degeneration and in the other to incipient cataract, bilateral choroiditis and unilateral macular hemorrhages. In the older patient, cataract surgery was technically successful, in the younger, the etiology of the fundus lesion could have been either myopia or arteriosclerosis or chronic pulmonary infection. (6 figures, references)

K. W. Ascher.

Gelfand, M. L. **Visual symptoms after digitoxin therapy.** J.A.M.A. **147**:1231-1233, Nov. 24, 1951.

Digitoxin is preferable to digitalis leaf in the treatment of congestive heart failure and arrhythmias. Oral dosage of 1.2 mg. and a maintenance dose of 0.2 mg. are generally safe, although digitoxin poisoning has occurred. Ocular symptoms from digitalis poisoning, and, more recently from digitoxin ingestion, have been recognized since 1785. Visual disorders after digitoxin therapy, without other signs of toxicity, were seen in the four cases reported. A man, 69 years old, with heart failure following an old infarction, developed blurred vision with "flickering lights" after two weeks' treatment with digitoxin. The symptoms disappeared when the digitoxin was stopped. A man 70 years old, with congestive heart failure, had blurred vision and white spots before the eyes. In daylight outdoor objects seemed covered with snow. When the drug was stopped the symptoms disappeared but reappeared when it was resumed. Two women with congestive heart failure, one 72 years old, the other 78 years old, complained of visual disturbances similar to those cited above, but both patients could tolerate a dose of 0.1 mg. digitoxin without untoward effects. Patients on digitoxin therapy should be carefully watched for visual symptoms, especially unexplained blurring of vision and disturbances in color perception.

Claude L. LaRue.

Pagliarani, N. **Brucella infection in man.** Ophthalmologica **122**:31-45, July, 1951.

After a fairly detailed review of the literature four cases of chronic inflammatory eye disease of presumably brucellar etiology are reported. The principal manifestations of the disease were arachnoiditis causing optic neuritis and abducens nerve palsy in the first case, uveitis combined with mild meningitis in the second and third, and bilateral dacryoadenitis in the fourth. Positive blood cultures were obtained in two of the cases. The hematological and serological findings were suggestive of brucellosis in all four cases.

Peter C. Kronfeld.

Pillat, A. **Microscopic findings in congenital ocular toxoplasmosis.** Wien. klin. Wchnschr. **63**:628-631, 1951.

Congenital ocular toxoplasmosis is primarily a retinal disease with direct invasion of the retinal structures by toxoplasma. The choroid is involved only secondarily and to a lesser degree. Necrosis and atrophy predominate over the relatively mild inflammation which is characterized by hyperemia and lymphocytosis. The eye of an 18-day-old infant who had died from generalized toxoplasmosis showed these histological changes. Toxoplasmas were found in the retina, choroid and posterior ciliary arteries, but the iris and ciliary body were free from disease. (4 figures, references)

Max Hirschfelder.

Rieger, H. **Toxoplasmosis.** Wien. klin. Wchnschr. **63**:680-683, 1951.

This postgraduate lecture summarizes the history of toxoplasmosis. The clinical symptoms and findings in congenital toxoplasmosis with visceral and cerebral manifestations are described; the course of extrauterine infection is discussed with the typhus-like signs in generalized cases, and the picture of uveitis in involvement of the eye is given. The possibility of toxoplasma transfer from animals like rats, dogs and mice to human beings is considered. (References)

Max Hirschfelder.

Wegner, W., and Zintz, R. **Chemotherapy of tuberculosis of the eye. Preliminary report.** Klin. Monatsbl. f. Augenh. 119:350-365, 1951.

The 300 carefully selected patients were treated and observed for about 14 months. There was an iridocyclitis in 147 eyes, a uveitis in 64, a choroiditis in 33, and a periphlebitis of the retina in 56. A more or less extensive tuberculosis of the lungs was present in 215 of the patients. Treatment consisted in the administration of Conteben or para-amino-salicylic acid (PAS) or both drugs together. Favorable results were definitely obtained in 10.5 percent of all cases. Agranulocytosis developed in 3 of 148 cases treated with Conteben. Several other patients had leucopenia. The results seemed to be somewhat better when Conteben was combined with PAS. Ernst Schmerl.

19

CONGENITAL DEFORMITIES, HEREDITY

Falls, H. F. **Role of heredity in ophthalmology.** New York State J. Med. 51:2624-2627, Nov. 15, 1951.

The nature, role and action of genes is briefly described and a method is outlined for studying the practical applications of heredity and for taking a genetic history. Thorough, complete histories of patients has helped in establishing the definite diagnosis of certain syndromes. Where a background of glaucoma exists, provocative tests and follow-up care are strongly advised. Possibly many ocular diseases of senility might be prevented by modifying the environment and daily life of persons predisposed by heredity to gout, diabetes and hypertension.

F. M. Crage.

vom Hofe, K. **Organ-hypersensitivity as observed in the eye.** Klin. Monatsbl. f. Augenh. 119:366-370, 1951.

The author gives a table which shows the familial tendency to affections of the eye in 10 families and points out that inflammatory eye disease in relatives may localize in different parts of the eye.

Ernst Schmerl.

Rieger, H. **The question of inheritance in retinal glioma.** Wien. klin. Wchnschr. 63:573-574, 1951.

The possibility that inheritance is a factor in retinal glioma has not yet been positively affirmed nor could it ever be completely rejected. Studies during the past twenty years seem to indicate that inheritance plays a part in the disease, perhaps due to an increased disposition of the body cells for mutative changes conditioned by the genes. Families in which an apparently single case of glioma appears should be investigated for general mutative characteristics of the entire body.

Max Hirschfelder.

Roussel, F. **Mandibular-facial dysostosis.** Ann. d'ocul. 184:788-802, Sept., 1951.

Receding jaw and a large mouth are frequent signs of the incomplete syndrome; deformities of the external and middle ear, malformations of the lids such as colobomata and ptosis, and abnormalities of head contours such as bird head are less frequent. At about the seventh week of fetal life defective development in the first and second branchial arches causes imperfections of the lower face. The author reports cases from four successive generations in a family predisposed to mandibular-facial dysostosis by irregular dominant heredity. Each succeeding generation had more manifestations and in the fourth generation a case of the complete syndrome appeared.

Chas. A. Bahn.

Wexler, David. **Ocular histology in Hurler's disease (gargoylism).** A.M.A. Arch. Ophth. **46**:14-21, July, 1951.

Hurler's syndrome consists of chondrodystrophic changes in the skeleton, corneal opacities, enlargement of the spleen, and mental deficiency. Because of the characteristic facies of the patient it is also known as gargoylism of which approximately 50 cases have been reported; in 16 autopsies were performed and the organs studied. In the case reported there were striking alterations in the connective tissue of the viscera, cardiovascular system and skeleton. The corneal lesion was easily demonstrated and consisted of a deposit of vacuolated cells beneath the epithelium and disruption of Bowman's layer. The sclera showed an infiltration of small, deeply staining cells and a thick deposit of intensely staining material between the scleral bundles, more solid than the cornea, and found uniformly between all the scleral bundles. There were alterations in the mesenchymal tissues, often associated with proliferation of collagenous fibers and sometimes with increase in ground substance in many of the organs. (8 figures) Edward J. Swets.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Foote, F. M., and Johnson, T. H. **Progress in preventing blindness.** New York State J. Med. **51**:2609-2612, Nov. 15, 1951.

Early in the century one third of the children in the state school for the blind at Batavia had had ophthalmia neonatorum; none of the 99 patients admitted in the past five years were blind because of this disease. Child blindness from lues has been reduced 50 percent in the United States during the last 12 years and blindness due to trauma 25 percent. However, there has been an increase in blindness from non-infectious prenatal causes. Retrolental fibroplasia has increased in importance because of successful efforts to save small premature babies. Early diagnosis, continued supervision of glaucoma, studies on retrolental fibroplasia and visual education in industry and technical schools are still important as aids in reducing the incidence of blindness.

F. M. Crage.

Nordenson, J. W. **Ophthalmic international standards, 1950.** Brit. J. Ophth. **35**: 496-501, Aug., 1951.

Reports of the commissions of the Ophthalmological Congresses are chronologically presented. The regulations approved in 1950 are given in detail. The reader is referred to the original article for details. Orwyn H. Ellis.

Ophthalmic Miniature

The search for truth is in one way hard and in another easy. For it is evident that no one can master it fully nor miss it wholly. But each adds a little to our knowledge of Nature, and from all the facts assembled there arises a certain grandeur.

Aristotle.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received at least three months before the date of occurrence.

DEATHS

Dr. John Robert Walker, Carmel, California, died November 16, 1951, aged 77 years.

Robert R. Irwin, LL.D., Port Orchard, Washington, retired executive director of the American Foundation for the Blind (1929-1950), died at his home on December 12, 1951.

ANNOUNCEMENTS

MICHIGAN POSTGRADUATE PROGRAM

On April 21, 22, and 23, an ophthalmology conference will be held at Ann Arbor, Michigan, as part of the annual Michigan postgraduate program for graduates in medicine. Guest lecturers for the conference will be: Dr. Hermann Burian, University of Iowa, Iowa City; Dr. Alston Callahan, The Medical College of Alabama, Birmingham; Dr. John W. Henderson, Mayo Clinic, Rochester, Minnesota; Dr. A. E. Maumenee, Stanford University School of Medicine, San Francisco.

Resident lecturers will be: Dr. Jerome W. Conn, professor of internal medicine, Dr. Harold F. Falls, associate professor of ophthalmology, Dr. F. Bruce Fralick, professor of ophthalmology, and Dr. John Woodworth Henderson, assistant professor of ophthalmology, of the University of Michigan School of Medicine.

FLORIDA MEETING

The 13th annual meeting of the Florida Society of Ophthalmology and Otolaryngology will be held on Sunday, April 27, at the Hollywood Beach Hotel, Hollywood Beach.

The following papers will be presented: "Present day management of chronic suppurative otitis media," Dr. Arthur Juers, Miami (discussion by Dr. J. Brown Farrior, Tampa, and Dr. Dekle Taylor, Jacksonville); "Ocular neuroses," Dr. G. Taylor Gwathmey, Orlando (discussion by Dr. Shaler Richardson, Jacksonville, and Dr. Kenneth S. Whitmer, Miami).

"Selection of operative procedure in vertical muscle imbalances," Dr. Edward Dunlap, associate professor of ophthalmology, Cornell University, New York; and "Therapeutic approaches to the inner ear," Dr. Jerome A. Hilger, clinical assistant professor of otology, University of Minnesota School of Medicine.

Mr. Harry E. Simmons, executive director, will give the annual report of the Florida Council for the Blind, and Dr. James R. Nieder, Delray Beach, will present a movie on "Cataract extraction by erisophake."

Officers of the society are: President, Dr. Charles C. Grace, St. Augustine; president-elect, Dr. Joseph W. Taylor, Tampa: 1st vice-president, Dr. M. A. Lischkoff, Pensacola; 2nd vice-president, Dr. G. T. Gwathmey, Orlando; secretary-treasurer, Dr. Carl S. McLemore, Orlando.

MISCELLANEOUS

TORONTO EYE-SURGERY COURSE

The University of Toronto, Faculty of Medicine, will give a refresher course in eye surgery from March 31 to April 4, at which the guest surgeons will be: Dr. Daniel B. Kirby, New York, and Mr. T. Keith Lyle, London. Dr. A. E. MacDonald, Dr. J. S. Crawford, Dr. J. C. Hill, Dr. A. L. Morgan, Dr. R. G. C. Kelly, Dr. W. R. F. Luke, Dr. H. M. Macrae, and Dr. T. H. Hodgson will also participate in the program.

OREGON ACADEMY MEETING

At the annual spring convention of the Oregon Academy of Ophthalmology and Otolaryngology in Portland, March 24 to 28, Dr. Frederick C. Cordes, San Francisco, will present the third John E. Weeks Memorial Lecture in Ophthalmology. Dr. Cordes's subject will be "The visual prognosis in diabetes."

In addition to Dr. Cordes, the other guest speakers will be: Dr. Philip E. Meltzer, Tufts College Medical School, Boston; Dr. Francis A. Lederer and Dr. William F. Hughes, Jr., University of Illinois College of Medicine, Chicago.

PITTSBURGH COURSE IN SLITLAMP MICROSCOPY

From February 25 through February 29 at the Montefiore Hospital, Pittsburgh, the 20th annual course in slitlamp microscopy was given by the department of ophthalmology under the direction of Dr. Harvey E. Thorpe and associates. Included in the program were courses on the management of intraocular foreign bodies, on glaucoma surgery, and on application of ACTH and cortisone in ophthalmology.

Visiting lecturers in gonioscopy were Dr. James H. Allen, New Orleans, and Mr. Lee Allen, Iowa City. The course was sponsored by the Committee on Graduate Education, Allegheny County Medical Society.

GLAUCOMA RESEARCH GRANT

Vital research on glaucoma will be carried on at the University of Cincinnati College of Medicine,

Cincinnati, Ohio, through 1954 with the aid of a $23,488 grant from the Surgeon General, university officials have announced. The grant was awarded Dr. Charles K. W. Ascher, university assistant professor of ophthalmology, who for many years has been interested in glaucoma research.

Plans for the project call for attempts to determine further explanation of the mechanism of the disease process and the action of drugs on the diseased eye, according to Dr. Ascher, who was recommended to the Surgeon General as recipient of the grant by the National Advisory Neurological Diseases and Blindness Council.

Assisting Dr. Ascher in the project will be Dr. Edward J. Glaser and Dr. John C. Fuhs, research associates, and Dr. James L. Stambaugh, Jr., senior resident, all of the university's department of ophthalmology, and Dr. William M. Spurgeon, mathematical consultant.

Plastic spectacle lenses

Cataract bifocals weighing only half as much as those of glass have been announced by Robert Graham, research director of the Armorlite Lens Company, Pasadena, California. The lenses are cast from a recently developed optical resin which is highly resistant to abrasion. Spherocylindric as well as spherical corrections are produced throughout a wide range. The bifocals are of one-piece construction with round segments 21 mm. across.

Fireworks law

Every ophthalmologist has had his heart touched by the needless blinding of children by fireworks and will be glad to learn that some states have reduced such losses to a minimum through laws prohibiting the sale and use of dangerous fireworks except for supervised public display.

But casualties are again on the increase. Dangerous fireworks are being shipped into states in violation of state laws. An interstate law can stop this traffic. Therefore eye doctors generally will approve a measure introduced by Congresswoman Marguerite Stitt Church to bring this about.

Approval is not enough, however. Letters must be sent to Washington urging prompt and favorable action. The bill was in subcommittee from June to January and, on January 23, the subcommittee voted unanimously to recommend favorable action by the full judiciary committee. If it reaches the floor of the House, it will probably pass overwhelmingly. The JOURNAL therefore urges that you write to the Hon. Emanuel Celler, chairman of the Judiciary Committee in the House and to your own representative urging prompt and favorable action of H.R. 4528. Address them care of the House of Representatives, Washington 25, D.C.

Wintersteiner-Elschnig slide collection

Dr. Milton R. Israel of the department of ophthalmology, St. Louis University School of Medicine, has completely catalogued some 15,000 slides of the Wintersteiner-Elschnig collection during the past year.

The collection, which has been a possession of the university for over 30 years, provides a picture of most types of eye diseases recognizable by specialists. Photomicrographs of the slides are to be made so that they may be sent to scientists throughout the country on request.

St. Louis University acquired the collection from Dr. Wintersteiner's widow after Dr. Joseph M. Keller and Dr. William H. Luedde had seen the collection while they were studying in Vienna. Although some of the slides were made as long ago as 1890, each one is perfectly preserved with the original labels still intact.

With the collection came a bibliography with a history of the diseases in the eyes which had been sectioned, together with a general description of the groups of diseases but no description of the individual slides.

Dr. E. V. L. Brown, professor of ophthalmology at the University of Illinois, Chicago, and this year's recipient of the Leslie Dana medal, recently explained some of the slides in his lecture on "Dr. Wintersteiner, his teaching methods and procedures."

Symposium on ACTH and cortisone

Dr. Greogory Shwartzman, chairman, Section on Microbiology, New York Academy of Medicine, has announced that a symposium on "The effect of ACTH and cortisone upon infection and resistance" will take place on March 27 and 28 at the New York Academy of Medicine.

Contributors to the symposium will be: Metabolism (Dr. F. L. Engel), Enzymatic reactions in rat tissues (Dr. W. W. Umbreit), Lymphoid tissue (Dr. W. E. Ehrich), Loose connective tissue (Dr. C. A. Ragan, Jr.), Antigen-antibody reactions (Dr. E. E. Fischel), Resistance to infections and tumor grafting (Dr. H. C. Stoerk), Bronchial asthma and rug idiosyncrasy (Dr. A. McGehee Harvey), Toxins and experimental streptococcus hemolyticus (Dr. L. Thomas), Spontaneous trypanasomiasis (Dr. A. Wolf), Experimental poliomyelitis (Dr. G. Shwartzman), Bacterial infections and malaria (Dr. N. Finland, Tuberculosis (Dr. M. B. Lurie), Infections of the eye (Dr. A. C. Woods), Experimental syphilis (Dr. T. B. Turner).

The meetings will be held in the academy building, 2 East 103rd St., New York, New York, and will be open to all who are interested.

East-Central research program

The East Central Section of the Association for Research in Ophthalmology held its annual meeting at Ann Arbor, Michigan, on February 1. The following papers were presented:

"The neurovascular mechanism controlling the ocular tension in congenital glaucoma of rabbits," Dr. Ernst Schmerl and Dr. Bernhard Steinberg, Toledo Hospital Institute of Medical Research; "Retinal vascular changes in diabetes mellitus," Dr. John J. Hartford, Cincinnati; "Direction sense of the eye," Elek J. Ludvigh, Ph.D., Kresge Eye Insti-

tute, Detroit; "An evaluation of aramine, a new mydriatic agent," Dr. E. P. Wickerham, Jr., and Dr. Jay G. Linn, Jr., University of Pittsburgh; "Experimental use of thrombin and plasma in corneal healing," Dr. C. William Weisser, Pittsburgh.

"Carbohydrate metabolism and energy relationships in the crystalline lens," Charles E. Frohman, Ph.D., and V. Everett Kinsey, Ph.D., Kresge Eye Institute, Detroit; "The effect of lobotomy and electroshock on intraocular pressure," Dr. Maria Arstikaitis and Dr. T. H. Hodgson, University of Toronto; "Hemispheric photic driving in homonymous hemianopias," Dr. Andre Well and Dr. William A. Nosik, Western Reserve University.

"The relationship between perceived size and perceived distance," Glenn A. Fry, Ph.D., Ohio State University; "Diabetic cataracts," Dr. John W. Patterson, Western Reserve University; "The influence of viewing distance upon visual performance," H. R. Blackwell, Ph.D., University of Michigan; "The detection of intraocular tumors with radioactive phosphorous," Dr. Charles I. Thomas, Western Reserve University; "The nutritional supply of corneal regions in experimental animals: II. The corneal transparency problem and the tonicity of tears," Dr. Albert M. Potts, with the assistance of Mildred Orchen, Western Reserve University.

Dr. Frank H. Bethell, University of Michigan, was the guest speaker. The subject of his address was: "The role of isotopes in modern medicine."

Societies

Richmond officers

Officers of the Richmond (Virginia) Eye, Ear, Nose, and Throat Society are: President, Dr. Mason Smith; secretary-treasurer, Dr. C. N. Romaine. The society meets the first Tuesday of January, March, May, and October at the Commonwealth Club.

Annual research meeting

The Association for Research in Ophthalmology will hold its annual meeting jointly with the Section on Ophthalmology of the A.M.A. in Chicago, June 10 to 15.

Egyptian meeting

The annual meeting of the Ophthalmological Society of Egypt was held at the Memorial Ophthalmic Laboratory, Giza, Egypt, on March 14 and 15.

Puget Sound Academy officers

Officers of the Puget Sound Academy of Ophthalmology and Otolaryngology for 1952 are: President, Dr. H. Frederick Thorlakson; secretary, Dr. Willard F. Goff.

Central Illinois meeting

The next meeting of the Central Illinois Society of Ophthalmology and Otolaryngology will be held at the Abraham Lincoln Hotel in Springfield, Illinois, on March 28, 29, and 30. The guest speakers will be Dr. James B. Costen of St. Louis and Dr. Trygve Gundersen of Boston.

Georgia meeting

The Georgia Society of Ophthalmology and Otolaryngology held its annual meeting at the General Oglethorpe Hotel on Wilmington Island, Savannah, on March 7 and 8. Guest speakers on the eye program were: Dr. Murray F. McCaslin, Pittsburgh, "Selection of anesthesia in ophthalmology," Dr. Joseph S. Haas, Chicago, "Differential diagnosis of the primary glaucomas" and "Provocative tests in glaucoma"; Dr. J. Conrad Gemeroy, Detroit, "External diseases of the eye" and "Management of metallic intraocular foreign bodies."

Brooklyn program

At the 119th regular meeting of the Brooklyn Ophthalmological Society, Dr. Sidney Fox presented a paper on "Surgery of the adnexa of the eye," and Dr. Abraham Kornzweig (by invitation) spoke on "Embryology of the eye." Dr. Edwin N. Beery discussed, "Controlled ciliary spasm for problems in divergence."

Florida program

The following program was presented at the fifth midwinter meeting of the Florida Society of Ophthalmology and Otolaryngology: Call to order, Dr. Charles Grace, president, St. Augustine; presentation of past president's key to Dr. Renfro Duke, Tampa; "Adrenal steroid therapy in ocular surgery," Dr. John McLean, professor of ophthalmology, Cornell University, New York; "Neurolysis for hemifacial spasm," Dr. Henry L. Williams, professor of otolaryngology, Mayo Foundation Graduate School, Rochester, Minnesota.

Personals

Dr. Derrick Vail, Chicago, will leave the end of March for Dublin, Ireland, where he will present the annual Montgomery Lecture of the Royal College of Surgeons of Ireland on April 17. The Ophthalmological Society of the United Kingdom will hold its annual meeting at the same time and place.

On January 25, Dr. Girolamo Bonaccolto was the guest speaker at the Yale University School of Medicine Postgraduate Courses in Ophthalmology. His subject was "Surgical technique of extraction of dislocated lens" with illustrations in colored film.

Dr. Joseph I. Pascal has been appointed lecturer in ophthalmology at the Brooklyn Eye and Ear Hospital.

At the IV Pan-American Congress of Ophthalmology at Mexico City, Dr. Arthur A. Knapp, New York, presented a paper on "The ocular criteria for surgical decision: The physiologic bases."

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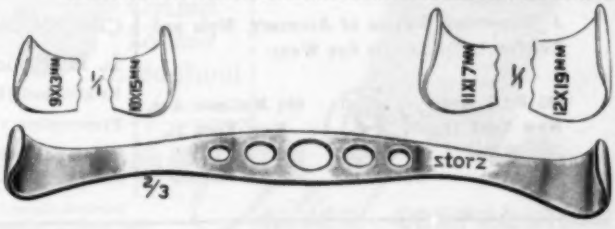

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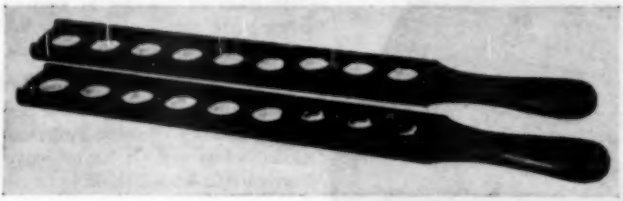

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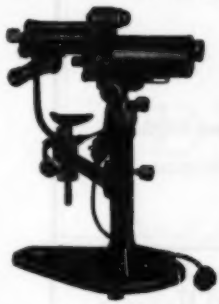

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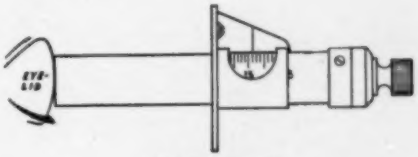

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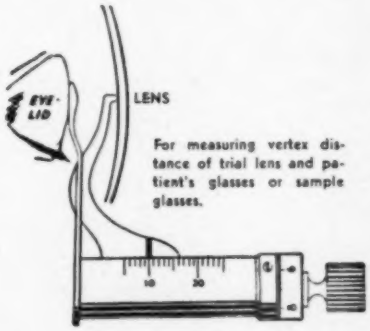

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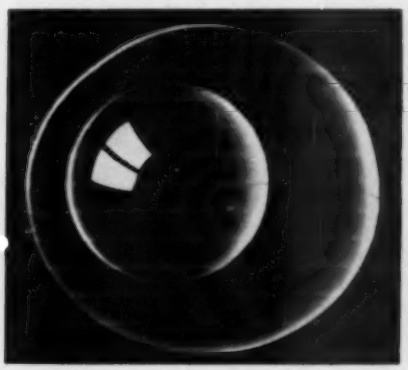

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